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ISOLATED HUMAN TRANSPORTER PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN TRANSPORTER PROTEINS, AND USES THEREOF

FIELD OF THE INVENTION

The present invention is in the field of transporter proteins that are related to the Na+independent transporter subfamily, recombinant DNA molecules, and protein production.

The present invention specifically provides novel peptides and proteins that effect ligand transport and nucleic acid molecules encoding such peptide and protein molecules, all of which are useful in the development of human therapeutics and diagnostic compositions and methods.

BACKGROUND OF THE INVENTION

Transporters

Transporter proteins regulate many different functions of a cell, including cell proliferation, differentiation, and signaling processes, by regulating the flow of molecules such as ions and macromolecules, into and out of cells. Transporters are found in the plasma membranes of virtually every cell in eukaryotic organisms. Transporters mediate a variety of cellular functions including regulation of membrane potentials and absorption and secretion of molecules and ion across cell membranes. When present in intracellular membranes of the Golgi apparatus and endocytic vesicles, transporters, such as chloride channels, also regulate organelle pH. For a review, see Greger, R. (1988) Annu. Rev. Physiol. 50:111-122.

Transporters are generally classified by structure and the type of mode of action. In addition, transporters are sometimes classified by the molecule type that is transported, for example, sugar transporters, chlorine channels, potassium channels, etc. There may be many classes of channels for transporting a single type of molecule (a detailed review of channel types can be found at Alexander, S.P.H. and J.A. Peters: Receptor and transporter nomenclature supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 (1997).

The following general classification scheme is known in the art and is followed in the present discoveries.

Channel-type transporters. Transmembrane channel proteins of this class are ubiquitously found in the membranes of all types of organisms from bacteria to higher

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eukaryotes. Transport systems of this type catalyze facilitated diffusion (by an energy-independent process) by passage through a transmembrane aqueous pore or channel without evidence for a carrier-mediated mechanism. These channel proteins usually consist largely of a-helical spanners, although b-strands may also be present and may even comprise the channel. However, outer membrane porin-type channel proteins are excluded from this class and are instead included in class 9.

Carrier-type transporters. Transport systems are included in this class if they utilize a carrier-mediated process to catalyze uniport (a single species is transported by facilitated diffusion), antiport (two or more species are transported in opposite directions in a tightly coupled process, not coupled to a direct form of energy other than chemiosmotic energy) and/or symport (two or more species are transported together in the same direction in a tightly coupled process, not coupled to a direct form of energy other than chemiosmotic energy).

Pyrophosphate bond hydrolysis-driven active transporters. Transport systems are included in this class if they hydrolyze pyrophosphate or the terminal pyrophosphate bond in ATP or another nucleoside triphosphate to drive the active uptake and/or extrusion of a solute or solutes. The transport protein may or may not be transiently phosphorylated, but the substrate is not phosphorylated.

PEP-dependent, phosphoryl transfer-driven group translocators. Transport systems of the bacterial phosphoenolpyruvate:sugar phosphotransferase system are included in this class. The product of the reaction, derived from extracellular sugar, is a cytoplasmic sugar-phosphate.

Decarboxylation-driven active transporters. Transport systems that drive solute (e.g., ion) uptake or extrusion by decarboxylation of a cytoplasmic substrate are included in this class.

Oxidoreduction-driven active transporters. Transport systems that drive transport of a solute (e.g., an ion) energized by the flow of electrons from a reduced substrate to an oxidized substrate are included in this class.

Light-driven active transporters. Transport systems that utilize light energy to drive transport of a solute (e.g., an ion) are included in this class.

Mechanically-driven active transporters. Transport systems are included in this class if they drive movement of a cell or organelle by allowing the flow of ions (or other solutes) through the membrane down their electrochemical gradients.

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Outer-membrane porins (of b-structure). These proteins form transmembrane pores or channels that usually allow the energy independent passage of solutes across a membrane. The transmembrane portions of these proteins consist exclusively of b-strands that form a b-barrel. These porin-type proteins are found in the outer membranes of Gram-negative bacteria, mitochondria and eukaryotic plastids.

Methyltransferase-driven active transporters. A single characterized protein currently falls into this category, the Na+-transporting methyltetrahydromethanopterin:coenzyme M methyltransferase.

Non-ribosome-synthesized channel-forming peptides or peptide-like molecules. These molecules, usually chains of L- and D-amino acids as well as other small molecular building blocks such as lactate, form oligomeric transmembrane ion channels. Voltage may induce channel formation by promoting assembly of the transmembrane channel. These peptides are often made by bacteria and fungi as agents of biological warfare.

Non-Proteinaceous Transport Complexes. Ion conducting substances in biological membranes that do not consist of or are not derived from proteins or peptides fall into this category.

Functionally characterized transporters for which sequence data are lacking.

Transporters of particular physiological significance will be included in this category even though a family assignment cannot be made.

Putative transporters in which no family member is an established transporter.

Putative transport protein families are grouped under this number and will either be classified elsewhere when the transport function of a member becomes established, or will be eliminated from the TC classification system if the proposed transport function is disproven.

These families include a member or members for which a transport function has been suggested, but evidence for such a function is not yet compelling.

Auxiliary transport proteins. Proteins that in some way facilitate transport across one or more biological membranes but do not themselves participate directly in transport are included in this class. These proteins always function in conjunction with one or more transport proteins. They may provide a function connected with energy coupling to transport, play a structural role in complex formation or serve a regulatory function.

Transporters of unknown classification. Transport protein families of unknown classification are grouped under this number and will be classified elsewhere when the transport process and energy coupling mechanism are characterized. These families include

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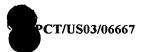
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at least one member for which a transport function has been established, but either the mode of transport or the energy coupling mechanism is not known.

Ion channels

An important type of transporter is the ion channel. Ion channels regulate many different cell proliferation, differentiation, and signaling processes by regulating the flow of ions into and out of cells. Ion channels are found in the plasma membranes of virtually every cell in eukaryotic organisms. Ion channels mediate a variety of cellular functions including regulation of membrane potentials and absorption and secretion of ion across epithelial membranes. When present in intracellular membranes of the Golgi apparatus and endocytic vesicles, ion channels, such as chloride channels, also regulate organelle pH. For a review, see Greger, R. (1988) Annu. Rev. Physiol. 50:111-122.

Ion channels are generally classified by structure and the type of mode of action. For example, extracellular ligand gated channels (ELGs) are comprised of five polypeptide subunits, with each subunit having 4 membrane spanning domains, and are activated by the binding of an extracellular ligand to the channel. In addition, channels are sometimes classified by the ion type that is transported, for example, chlorine channels, potassium channels, etc. There may be many classes of channels for transporting a single type of ion (a detailed review of channel types can be found at Alexander, S.P.H. and J.A. Peters (1997). Receptor and ion channel nomenclature supplement. Trends Pharmacol. Sci., Elsevier, pp. 65-68 and http://www-biology.ucsd.edu/~msaier/transport/toc.html.

There are many types of ion channels based on structure. For example, many ion channels fall within one of the following groups: extracellular ligand-gated channels (ELG), intracellular ligand-gated channels (ILG), inward rectifying channels (INR), intercellular (gap junction) channels, and voltage gated channels (VIC). There are additionally recognized other channel families based on ion-type transported, cellular location and drug sensitivity. Detailed information on each of these, their activity, ligand type, ion type, disease association, drugability, and other information pertinent to the present invention, is well known in the art.

Extracellular ligand-gated channels, ELGs, are generally comprised of five polypeptide subunits, Unwin, N. (1993), Cell 72: 31-41; Unwin, N. (1995), Nature 373: 37-43; Hucho, F., et al., (1996) J. Neurochem. 66: 1781-1792; Hucho, F., et al., (1996) Eur. J. Biochem. 239: 539-557; Alexander, S.P.H. and J.A. Peters (1997), Trends Pharmacol. Sci.,

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Elsevier, pp. 4-6; 36-40; 42-44; and Xue, H. (1998) J. Mol. Evol. 47: 323-333. Each subunit has 4 membrane spanning regions: this serves as a means of identifying other members of the ELG family of proteins. ELG bind a ligand and in response modulate the flow of ions. Examples of ELG include most members of the neurotransmitter-receptor family of proteins, e.g., GABAI receptors. Other members of this family of ion channels include glycine receptors, ryandyne receptors, and ligand gated calcium channels.

The Voltage-gated Ion Channel (VIC) Superfamily

Proteins of the VIC family are ion-selective channel proteins found in a wide range of bacteria, archaea and eukaryotes Hille, B. (1992), Chapter 9: Structure of channel proteins; Chapter 20: Evolution and diversity. In: Ionic Channels of Excitable Membranes, 2nd Ed., Sinaur Assoc. Inc., Pubs., Sunderland, Massachusetts; Sigworth, F.J. (1993), Quart. Rev. Biophys. 27: 1-40; Salkoff, L. and T. Jegla (1995), Neuron 15: 489-492; Alexander, S.P.H. et al., (1997), Trends Pharmacol. Sci., Elsevier, pp. 76-84; Jan, L.Y. et al., (1997), Annu. Rev. Neurosci. 20: 91-123; Doyle, D.A, et al., (1998) Science 280: 69-77; Terlau, H. and W. Stühmer (1998), Naturwissenschaften 85: 437-444. They are often homo- or heterooligomeric structures with several dissimilar subunits (e.g., a1-a2-d-b Ca2+ channels, ab₁b₂ Na⁺ channels or (a)₄-b K⁺ channels), but the channel and the primary receptor is usually associated with the a (or a1) subunit. Functionally characterized members are specific for K⁺, Na⁺ or Ca²⁺. The K⁺ channels usually consist of homotetrameric structures with each a-subunit possessing six transmembrane spanners (TMSs). The al and a subunits of the Ca²⁺ and Na⁺ channels, respectively, are about four times as large and possess 4 units, each with 6 TMSs separated by a hydrophilic loop, for a total of 24 TMSs. These large channel proteins form heterotetra-unit structures equivalent to the homotetrameric structures of most K⁺ channels. All four units of the Ca²⁺ and Na⁺ channels are homologous to the single unit in the homotetrameric K⁺ channels. Ion flux via the eukaryotic channels is generally controlled by the transmembrane electrical potential (hence the designation, voltage-sensitive) although some are controlled by ligand or receptor binding.

Several putative K⁺-selective channel proteins of the VIC family have been identified in prokaryotes. The structure of one of them, the KcsA K⁺ channel of *Streptomyces lividans*, has been solved to 3.2 Å resolution. The protein possesses four identical subunits, each with two transmembrane helices, arranged in the shape of an inverted teepee or cone. The cone cradles the "selectivity filter" P domain in its outer end. The narrow selectivity filter is only 12 Å long, whereas the remainder of the channel is wider and lined with hydrophobic

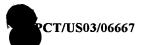
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residues. A large water-filled cavity and helix dipoles stabilize K^+ in the pore. The selectivity filter has two bound K^+ ions about 7.5 Å apart from each other. Ion conduction is proposed to result from a balance of electrostatic attractive and repulsive forces.

In eukaryotes, each VIC family channel type has several subtypes based on pharmacological and electrophysiological data. Thus, there are five types of Ca²⁺ channels (L. N. P. O and T). There are at least ten types of K⁺ channels, each responding in different ways to different stimuli: voltage-sensitive [Ka, Kv, Kvr, Kvs and Ksr], Ca²⁺-sensitive [BK_{Ca}, IK_{Ca} and SK_{Ca}] and receptor-coupled [K_M and K_{ACh}]. There are at least six types of Na⁺ channels (I, II, III, µ1, H1 and PN3). Tetrameric channels from both prokaryotic and eukaryotic organisms are known in which each a-subunit possesses 2 TMSs rather than 6, and these two TMSs are homologous to TMSs 5 and 6 of the six TMS unit found in the voltage-sensitive channel proteins. KcsA of S. lividans is an example of such a 2 TMS channel protein. These channels may include the K_{Na} (Na⁺-activated) and K_{Vol} (cell volumesensitive) K⁺ channels, as well as distantly related channels such as the Tok1 K⁺ channel of yeast, the TWIK-1 inward rectifier K⁺ channel of the mouse and the TREK-1 K⁺ channel of the mouse. Because of insufficient sequence similarity with proteins of the VIC family, inward rectifier K⁺ IRK channels (ATP-regulated; G-protein-activated) which possess a P domain and two flanking TMSs are placed in a distinct family. However, substantial sequence similarity in the P region suggests that they are homologous. The b, g and d subunits of VIC family members, when present, frequently play regulatory roles in channel activation/deactivation.

The Epithelial Na⁺ Channel (ENaC) Family

The ENaC family consists of over twenty-four sequenced proteins (Canessa, C.M., et al., (1994), Nature 367: 463-467, Le, T. and M.H. Saier, Jr. (1996), Mol. Membr. Biol. 13: 149-157; Garty, H. and L.G. Palmer (1997), Physiol. Rev. 77: 359-396; Waldmann, R., et al., (1997), Nature 386: 173-177; Darboux, I., et al., (1998), J. Biol. Chem. 273: 9424-9429; Firsov, D., et al., (1998), EMBO J. 17: 344-352; Horisberger, J.-D. (1998). Curr. Opin. Struc. Biol. 10: 443-449). All are from animals with no recognizable homologues in other eukaryotes or bacteria. The vertebrate ENaC proteins from epithelial cells cluster tightly together on the phylogenetic tree: voltage-insensitive ENaC homologues are also found in the brain. Eleven sequenced *C. elegans* proteins, including the degenerins, are distantly related to the vertebrate proteins as well as to each other. At least some of these proteins form part of a mechano-transducing complex for touch sensitivity. The homologous *Helix*

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aspersa (FMRF-amide)-activated Na⁺ channel is the first peptide neurotransmitter-gated ionotropic receptor to be sequenced.

Protein members of this family all exhibit the same apparent topology, each with N-and C-termini on the inside of the cell, two amphipathic transmembrane spanning segments, and a large extracellular loop. The extracellular domains contain numerous highly conserved cysteine residues. They are proposed to serve a receptor function.

Mammalian ENaC is important for the maintenance of Na⁺ balance and the regulation of blood pressure. Three homologous ENaC subunits, alpha, beta, and gamma, have been shown to assemble to form the highly Na ⁺-selective channel. The stoichiometry of the three subunits is alpha₂ beta1, gamma1 in a heterotetrameric architecture.

The Glutamate-gated Ion Channel (GIC) Family of Neurotransmitter Receptors

Members of the GIC family are heteropentameric complexes in which each of the 5 subunits is of 800-1000 amino acyl residues in length (Nakanishi, N., et al, (1990), Neuron 5: 569-581; Unwin, N. (1993), Cell 72: 31-41; Alexander, S.P.H. and J.A. Peters (1997) Trends Pharmacol. Sci., Elsevier, pp. 36-40). These subunits may span the membrane three or five times as putative a-helices with the N-termini (the glutamate-binding domains) localized extracellularly and the C-termini localized cytoplasmically. They may be distantly related to the ligand-gated ion channels, and if so, they may possess substantial b-structure in their transmembrane regions. However, homology between these two families cannot be established on the basis of sequence comparisons alone. The subunits fall into six subfamilies: a, b, g, d, e and z.

The GIC channels are divided into three types: (1) a-amino-3-hydroxy-5-methyl-4-isoxazole propionate (AMPA)-, (2) kainate- and (3) N-methyl-D-aspartate (NMDA)-selective glutamate receptors. Subunits of the AMPA and kainate classes exhibit 35-40% identity with each other while subunits of the NMDA receptors exhibit 22-24% identity with the former subunits. They possess large N-terminal, extracellular glutamate-binding domains that are homologous to the periplasmic glutamine and glutamate receptors of ABC-type uptake permeases of Gram-negative bacteria. All known members of the GIC family are from animals. The different channel (receptor) types exhibit distinct ion selectivities and conductance properties. The NMDA-selective large conductance channels are highly permeable to monovalent cations and Ca²⁺. The AMPA- and kainate-selective ion channels are permeable primarily to monovalent cations with only low permeability to Ca²⁺.

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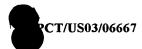
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The Chloride Channel (ClC) Family

The CIC family is a large family consisting of dozens of sequenced proteins derived from Gram-negative and Gram-positive bacteria, cyanobacteria, archaea, yeast, plants and animals (Steinmeyer, K., et al., (1991), Nature 354: 301-304; Uchida, S., et al., (1993), J. Biol. Chem. 268: 3821-3824; Huang, M.-E., et al., (1994), J. Mol. Biol. 242: 595-598; Kawasaki, M., et al, (1994), Neuron 12: 597-604; Fisher, W.E., et al., (1995), Genomics. 29:598-606; and Foskett, J.K. (1998), Annu. Rev. Physiol. 60: 689-717). These proteins are essentially ubiquitous, although they are not encoded within genomes of Haemophilus influenzae, Mycoplasma genitalium, and Mycoplasma pneumoniae. Sequenced proteins vary in size from 395 amino acyl residues (M. jannaschii) to 988 residues (man). Several organisms contain multiple ClC family paralogues. For example, Synechocystis has two paralogues, one of 451 residues in length and the other of 899 residues. Arabidopsis thaliana has at least four sequenced paralogues, (775-792 residues), humans also have at least five paralogues (820-988 residues), and C. elegans also has at least five (810-950 residues). There are nine known members in mammals, and mutations in three of the corresponding genes cause human diseases. E. coli, Methanococcus jannaschii and Saccharomyces cerevisiae only have one ClC family member each. With the exception of the larger Synechocystis paralogue, all bacterial proteins are small (395-492 residues) while all eukaryotic proteins are larger (687-988 residues). These proteins exhibit 10-12 putative transmembrane a-helical spanners (TMSs) and appear to be present in the membrane as homodimers. While one member of the family, Torpedo ClC-O, has been reported to have two channels, one per subunit, others are believed to have just one.

All functionally characterized members of the ClC family transport chloride, some in a voltage-regulated process. These channels serve a variety of physiological functions (cell volume regulation; membrane potential stabilization; signal transduction; transepithelial transport, etc.). Different homologues in humans exhibit differing anion selectivities, i.e., ClC4 and ClC5 share a $NO_3^- > Cl^- > Br^- > \Gamma$ conductance sequence, while ClC3 has an $\Gamma >$ Cl⁻ selectivity. The ClC4 and ClC5 channels and others exhibit outward rectifying currents with currents only at voltages more positive than +20mV.

Animal Inward Rectifier K⁺ Channel (IRK-C) Family

IRK channels possess the "minimal channel-forming structure" with only a P domain, characteristic of the channel proteins of the VIC family, and two flanking transmembrane

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spanners (Shuck, M.E., et al., (1994), J. Biol. Chem. 269: 24261-24270; Ashen, M.D., et al., (1995), Am. J. Physiol. 268: H506-H511; Salkoff, L. and T. Jegla (1995), Neuron 15: 489-492; Aguilar-Bryan, L., et al., (1998), Physiol. Rev. 78: 227-245; Ruknudin, A., et al., (1998), J. Biol. Chem. 273: 14165-14171). They may exist in the membrane as homo-or heterooligomers. They have a greater tendency to let K⁺ flow into the cell than out. Voltagedependence may be regulated by external K⁺, by internal Mg²⁺, by internal ATP and/or by G-proteins. The P domains of IRK channels exhibit limited sequence similarity to those of the VIC family, but this sequence similarity is insufficient to establish homology. Inward rectifiers play a role in setting cellular membrane potentials, and the closing of these channels upon depolarization permits the occurrence of long duration action potentials with a plateau phase. Inward rectifiers lack the intrinsic voltage sensing helices found in VIC family channels. In a few cases, those of Kirl.la and Kir6.2, for example, direct interaction with a member of the ABC superfamily has been proposed to confer unique functional and regulatory properties to the heteromeric complex, including sensitivity to ATP. The SUR1 sulfonylurea receptor (spQ09428) is the ABC protein that regulates the Kir6.2 channel in response to ATP, and CFTR may regulate Kirl.1a. Mutations in SUR1 are the cause of familial persistent hyperinsulinemic hypoglycemia in infancy (PHHI), an autosomal recessive disorder characterized by unregulated insulin secretion in the pancreas.

ATP-gated Cation Channel (ACC) Family

Members of the ACC family (also called P2X receptors) respond to ATP, a functional neurotransmitter released by exocytosis from many types of neurons (North, R.A. (1996), Curr. Opin. Cell Biol. 8: 474-483; Soto, F., M. Garcia-Guzman and W. Stühmer (1997), J. Membr. Biol. 160: 91-100). They have been placed into seven groups (P2X₁ - P2X₇) based on their pharmacological properties. These channels, which function at neuronneuron and neuron-smooth muscle junctions, may play roles in the control of blood pressure and pain sensation. They may also function in lymphocyte and platelet physiology. They are found only in animals.

The proteins of the ACC family are quite similar in sequence (>35% identity), but they possess 380-1000 amino acyl residues per subunit with variability in length localized primarily to the C-terminal domains. They possess two transmembrane spanners, one about 30-50 residues from their N-termini, the other near residues 320-340. The extracellular receptor domains between these two spanners (of about 270 residues) are well conserved with numerous conserved glycyl and cysteyl residues. The hydrophilic C-termini vary in

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length from 25 to 240 residues. They resemble the topologically similar epithelial Na⁺ channel (ENaC) proteins in possessing (a) N- and C-termini localized intracellularly, (b) two putative transmembrane spanners, (c) a large extracellular loop domain, and (d) many conserved extracellular cysteyl residues. ACC family members are, however, not demonstrably homologous with them. ACC channels are probably hetero- or homomultimers and transport small monovalent cations (Me⁺). Some also transport Ca²⁺; a few also transport small metabolites.

The Ryanodine-Inositol 1,4,5-triphosphate Receptor Ca²⁺ Channel (RIR-CaC) Family

Ryanodine (Ry)-sensitive and inositol 1,4,5-triphosphate (IP3)-sensitive Ca²⁺-release channels function in the release of Ca²⁺ from intracellular storage sites in animal cells and thereby regulate various Ca²⁺ -dependent physiological processes (Hasan, G. et al., (1992) Development 116: 967-975; Michikawa, T., et al., (1994), J. Biol. Chem. 269: 9184-9189; Tunwell, R.E.A., (1996), Biochem. J. 318: 477-487; Lee, A.G. (1996) *Biomembranes*, Vol. 6, Transmembrane Receptors and Channels (A.G. Lee, ed.), JAI Press, Denver, CO., pp 291-326; Mikoshiba, K., et al., (1996) J. Biochem. Biomem. 6: 273-289). Ry receptors occur primarily in muscle cell sarcoplasmic reticular (SR) membranes, and IP3 receptors occur primarily in brain cell endoplasmic reticular (ER) membranes where they effect release of Ca²⁺ into the cytoplasm upon activation (opening) of the channel.

The Ry receptors are activated as a result of the activity of dihydropyridine-sensitive Ca²⁺ channels. The latter are members of the voltage-sensitive ion channel (VIC) family. Dihydropyridine-sensitive channels are present in the T-tubular systems of muscle tissues.

Ry receptors are homotetrameric complexes with each subunit exhibiting a molecular size of over 500,000 daltons (about 5,000 amino acyl residues). They possess C-terminal domains with six putative transmembrane a -helical spanners (TMSs). Putative pore-forming sequences occur between the fifth and sixth TMSs as suggested for members of the VIC family. The large N-terminal hydrophilic domains and the small C-terminal hydrophilic domains are localized to the cytoplasm. Low resolution 3-dimensional structural data are available. Mammals possess at least three isoforms that probably arose by gene duplication and divergence before divergence of the mammalian species. Homologues are present in humans and Caenorabditis elegans.

IP₃ receptors resemble Ry receptors in many respects. (1) They are homotetrameric complexes with each subunit exhibiting a molecular size of over 300,000 daltons (about 2,700 amino acyl residues). (2) They possess C-terminal channel domains that are

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homologous to those of the Ry receptors. (3) The channel domains possess six putative TMSs and a putative channel lining region between TMSs 5 and 6. (4) Both the large N-terminal domains and the smaller C-terminal tails face the cytoplasm. (5) They possess covalently linked carbohydrate on extracytoplasmic loops of the channel domains. (6) They have three currently recognized isoforms (types 1, 2, and 3) in mammals which are subject to differential regulation and have different tissue distributions.

IP₃ receptors possess three domains: N-terminal IP₃-binding domains, central coupling or regulatory domains and C-terminal channel domains. Channels are activated by IP₃ binding, and like the Ry receptors, the activities of the IP₃ receptor channels are regulated by phosphorylation of the regulatory domains, catalyzed by various protein kinases. They predominate in the endoplasmic reticular membranes of various cell types in the brain but have also been found in the plasma membranes of some nerve cells derived from a variety of tissues.

The channel domains of the Ry and IP₃ receptors comprise a coherent family that in spite of apparent structural similarities, do not show appreciable sequence similarity of the proteins of the VIC family. The Ry receptors and the IP₃ receptors cluster separately on the RIR-CaC family tree. They both have homologues in *Drosophila*. Based on the phylogenetic tree for the family, the family probably evolved in the following sequence: (1) A gene duplication event occurred that gave rise to Ry and IP₃ receptors in invertebrates. (2) Vertebrates evolved from invertebrates. (3) The three isoforms of each receptor arose as a result of two distinct gene duplication events. (4) These isoforms were transmitted to mammals before divergence of the mammalian species.

The Organellar Chloride Channel (O-ClC) Family

Proteins of the O-ClC family are voltage-sensitive chloride channels found in intracellular membranes but not the plasma membranes of animal cells (Landry, D, et al., (1993), J. Biol. Chem. 268: 14948-14955; Valenzuela, Set al., (1997), J. Biol. Chem. 272: 12575-12582; and Duncan, R.R., et al., (1997), J. Biol. Chem. 272: 23880-23886).

They are found in human nuclear membranes, and the bovine protein targets to the microsomes, but not the plasma membrane, when expressed in *Xenopus laevis* oocytes. These proteins are thought to function in the regulation of the membrane potential and in transepithelial ion absorption and secretion in the kidney. They possess two putative transmembrane a-helical spanners (TMSs) with cytoplasmic N- and C-termini and a large luminal loop that may be glycosylated. The bovine protein is 437 amino acyl residues in

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length and has the two putative TMSs at positions 223-239 and 367-385. The human nuclear protein is much smaller (241 residues). A *C. elegans* homologue is 260 residues long.

The present invention has a substantial similarity to rat small intestine Na+independent transporter for aromatic amino acids that designated as TAT1 (T-type amino acid transporter 1).

System T was originally characterized in human erythrocytes. It transports aromatic amino acids in a Na⁺-independent manner. Although it was once proposed that system T is a variant of system L which shows Na⁺-independent transport of neutral amino acids including aromatic amino acids, system T is distinct in that it accepts N-methyl amino acids whereas system L does not. Therefore, it is reasonable to assume that transporters subserving system T would belong to a different family with distinct mechanisms of substrate recognition.

The Na+-independent transporter is Na+-independent and low-affinity transport of aromatic amino acids such as tryptophan, tyrosine, and phenylalanine (Km values: approximately 5 mm), consistent with the properties of classical amino acid transport system T. TAT1 accepted some variations of aromatic side chains because it interacted with amino acid-related compounds such as 1-DOPA and 3-O-methyl-DOPA. TAT1 recognizes amino acid substrates as anions, because TAT1 accepted N-methyl- and N-acetyl-derivatives of aromatic amino acids but did not accept their methylesters. Consistent with this, TAT1 exhibited sequence similarity (approximately 30% identity at the amino acid level) to H+/monocarboxylate transporters. Different from H+/monocarboxylate transporters, however, TAT1 was not coupled with the H+ transport but it mediates an electroneutral facilitated diffusion. In rat small intestine TAT1 immunoreactivity was detected in the basolateral membrane of the epithelial cells suggesting its role in the transporter, see Kim et al., J Biol Chem 2001 May 18;276(20):17221-8.

Transporter proteins, particularly members of the Na+-independent transporter subfamily, are a major target for drug action and development. Accordingly, it is valuable to the field of pharmaceutical development to identify and characterize previously unknown transport proteins. The present invention advances the state of the art by providing previously unidentified human transport proteins.

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SUMMARY OF THE INVENTION

The present invention is based in part on the identification of amino acid sequences of human transporter peptides and proteins that are related to the Na+-independent transporter subfamily, as well as allelic variants and other mammalian orthologs thereof.

These unique peptide sequences, and nucleic acid sequences that encode these peptides, can be used as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins, and serve as targets for the development of human therapeutic agents that modulate transporter activity in cells and tissues that express the transporter.

Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues.

DESCRIPTION OF THE FIGURE SHEETS

FIGURE 1 provides the nucleotide sequence of a cDNA molecule or transcript sequence that encodes the transporter protein of the present invention. (SEQ ID NO:1) In addition structure and functional information is provided, such as ATG start, stop and tissue distribution, where available, that allows one to readily determine specific uses of inventions based on this molecular sequence. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues.

FIGURE 2 provides the predicted amino acid sequence of the transporter of the present invention. (SEQ ID NO:2) In addition structure and functional information such as protein family, function, and modification sites is provided where available, allowing one to readily determine specific uses of inventions based on this molecular sequence.

FIGURE 3 provides genomic sequences that span the gene encoding the transporter protein of the present invention. (SEQ ID NO:3) In addition structure and functional information, such as intron/exon structure, promoter location, etc., is provided where available, allowing one to readily determine specific uses of inventions based on this molecular sequence. 94 SNPs, including 10 indels, have been identified in the gene encoding the transporter protein provided by the present invention and are given in Figure 3.

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DETAILED DESCRIPTION OF THE INVENTION

General Description

The present invention is based on the sequencing of the human genome. During the sequencing and assembly of the human genome, analysis of the sequence information revealed previously unidentified fragments of the human genome that encode peptides that share structural and/or sequence homology to protein/peptide/domains identified and characterized within the art as being a transporter protein or part of a transporter protein and are related to the Na+-independent transporter subfamily. Utilizing these sequences, additional genomic sequences were assembled and transcript and/or cDNA sequences were isolated and characterized. Based on this analysis, the present invention provides amino acid sequences of human transporter peptides and proteins that are related to the Na+-independent transporter subfamily, nucleic acid sequences in the form of transcript sequences, cDNA sequences and/or genomic sequences that encode these transporter peptides and proteins, nucleic acid variation (allelic information), tissue distribution of expression, and information about the closest art known protein/peptide/domain that has structural or sequence homology to the transporter of the present invention.

In addition to being previously unknown, the peptides that are provided in the present invention are selected based on their ability to be used for the development of commercially important products and services. Specifically, the present peptides are selected based on homology and/or structural relatedness to known transporter proteins of the Na+-independent transporter subfamily and the expression pattern observed. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues.. The art has clearly established the commercial importance of members of this family of proteins and proteins that have expression patterns similar to that of the present gene. Some of the more specific features of the peptides of the present invention, and the uses thereof, are described herein, particularly in the Background of the Invention and in the annotation provided in the Figures, and/or are known within the art for each of the known Na+-independent transporter family or subfamily of transporter proteins.

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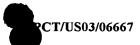
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Specific Embodiments

Peptide Molecules

The present invention provides nucleic acid sequences that encode protein molecules that have been identified as being members of the transporter family of proteins and are related to the Na+-independent transporter subfamily (protein sequences are provided in Figure 2, transcript/cDNA sequences are provided in Figures 1 and genomic sequences are provided in Figure 3). The peptide sequences provided in Figure 2, as well as the obvious variants described herein, particularly allelic variants as identified herein and using the information in Figure 3, will be referred herein as the transporter peptides of the present invention, transporter peptides, or peptides/proteins of the present invention.

The present invention provides isolated peptide and protein molecules that consist of, consist essentially of, or comprising the amino acid sequences of the transporter peptides disclosed in the Figure 2, (encoded by the nucleic acid molecule shown in Figure 1, transcript/cDNA or Figure 3, genomic sequence), as well as all obvious variants of these peptides that are within the art to make and use. Some of these variants are described in detail below.

As used herein, a peptide is said to be "isolated" or "purified" when it is substantially free of cellular material or free of chemical precursors or other chemicals. The peptides of the present invention can be purified to homogeneity or other degrees of purity. The level of purification will be based on the intended use. The critical feature is that the preparation allows for the desired function of the peptide, even if in the presence of considerable amounts of other components (the features of an isolated nucleic acid molecule is discussed below).

In some uses, "substantially free of cellular material" includes preparations of the peptide having less than about 30% (by dry weight) other proteins (i.e., contaminating protein), less than about 20% other proteins, less than about 10% other proteins, or less than about 5% other proteins. When the peptide is recombinantly produced, it can also be substantially free of culture medium, i.e., culture medium represents less than about 20% of the volume of the protein preparation.

The language "substantially free of chemical precursors or other chemicals" includes preparations of the peptide in which it is separated from chemical precursors or other chemicals that are involved in its synthesis. In one embodiment, the language "substantially free of chemical precursors or other chemicals" includes preparations of the transporter peptide having

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less than about 30% (by dry weight) chemical precursors or other chemicals, less than about 20% chemical precursors or other chemicals, less than about 10% chemical precursors or other chemicals, or less than about 5% chemical precursors or other chemicals.

The isolated transporter peptide can be purified from cells that naturally express it, purified from cells that have been altered to express it (recombinant), or synthesized using known protein synthesis methods. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. For example, a nucleic acid molecule encoding the transporter peptide is cloned into an expression vector, the expression vector introduced into a host cell and the protein expressed in the host cell. The protein can then be isolated from the cells by an appropriate purification scheme using standard protein purification techniques. Many of these techniques are described in detail below.

Accordingly, the present invention provides proteins that consist of the amino acid sequences provided in Figure 2 (SEQ ID NO:2), for example, proteins encoded by the transcript/cDNA nucleic acid sequences shown in Figure 1 (SEQ ID NO:1) and the genomic sequences provided in Figure 3 (SEQ ID NO:3). The amino acid sequence of such a protein is provided in Figure 2. A protein consists of an amino acid sequence when the amino acid sequence is the final amino acid sequence of the protein.

The present invention further provides proteins that consist essentially of the amino acid sequences provided in Figure 2 (SEQ ID NO:2), for example, proteins encoded by the transcript/cDNA nucleic acid sequences shown in Figure 1 (SEQ ID NO:1) and the genomic sequences provided in Figure 3 (SEQ ID NO:3). A protein consists essentially of an amino acid sequence when such an amino acid sequence is present with only a few additional amino acid residues, for example from about 1 to about 100 or so additional residues, typically from 1 to about 20 additional residues in the final protein.

The present invention further provides proteins that comprise the amino acid sequences provided in Figure 2 (SEQ ID NO:2), for example, proteins encoded by the transcript/cDNA nucleic acid sequences shown in Figure 1 (SEQ ID NO:1) and the genomic sequences provided in Figure 3 (SEQ ID NO:3). A protein comprises an amino acid sequence when the amino acid sequence is at least part of the final amino acid sequence of the protein. In such a fashion, the protein can be only the peptide or have additional amino acid molecules, such as amino acid residues (contiguous encoded sequence) that are naturally associated with it or heterologous amino acid residues/peptide sequences. Such a protein can have a few additional amino acid

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residues or can comprise several hundred or more additional amino acids. The preferred classes of proteins that are comprised of the transporter peptides of the present invention are the naturally occurring mature proteins. A brief description of how various types of these proteins can be made/isolated is provided below.

The transporter peptides of the present invention can be attached to heterologous sequences to form chimeric or fusion proteins. Such chimeric and fusion proteins comprise a transporter peptide operatively linked to a heterologous protein having an amino acid sequence not substantially homologous to the transporter peptide. "Operatively linked" indicates that the transporter peptide and the heterologous protein are fused in-frame. The heterologous protein can be fused to the N-terminus or C-terminus of the transporter peptide.

In some uses, the fusion protein does not affect the activity of the transporter peptide *per se*. For example, the fusion protein can include, but is not limited to, enzymatic fusion proteins, for example beta-galactosidase fusions, yeast two-hybrid GAL fusions, poly-His fusions, MYC-tagged, HI-tagged and Ig fusions. Such fusion proteins, particularly poly-His fusions, can facilitate the purification of recombinant transporter peptide. In certain host cells (e.g., mammalian host cells), expression and/or secretion of a protein can be increased by using a heterologous signal sequence.

A chimeric or fusion protein can be produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different protein sequences are ligated together in-frame in accordance with conventional techniques. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and re-amplified to generate a chimeric gene sequence (see Ausubel *et al.*, *Current Protocols in Molecular Biology*, 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST protein). A transporter peptide-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the transporter peptide.

As mentioned above, the present invention also provides and enables obvious variants of the amino acid sequence of the proteins of the present invention, such as naturally occurring mature forms of the peptide, allelic/sequence variants of the peptides, non-naturally occurring recombinantly derived variants of the peptides, and orthologs and paralogs of the peptides. Such variants can readily be generated using art-known techniques in the fields of recombinant

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nucleic acid technology and protein biochemistry. It is understood, however, that variants exclude any amino acid sequences disclosed prior to the invention.

Such variants can readily be identified/made using molecular techniques and the sequence information disclosed herein. Further, such variants can readily be distinguished from other peptides based on sequence and/or structural homology to the transporter peptides of the present invention. The degree of homology/identity present will be based primarily on whether the peptide is a functional variant or non-functional variant, the amount of divergence present in the paralog family and the evolutionary distance between the orthologs.

To determine the percent identity of two amino acid sequences or two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second amino acid or nucleic acid sequence for optimal alignment and non-homologous sequences can be disregarded for comparison purposes). In a preferred embodiment, at least 30%, 40%, 50%, 60%, 70%, 80%, or 90% or more of a reference sequence is aligned for comparison purposes. The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position (as used herein amino acid or nucleic acid "identity" is equivalent to amino acid or nucleic acid "homology"). The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

between two sequences can be accomplished using a mathematical algorithm.

(Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (available at http://www.gcg.com), using either a Blossom 62

The comparison of sequences and determination of percent identity and similarity

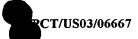
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matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (Devereux, J., et al., Nucleic Acids Res. 12(1):387 (1984)) (available at http://www.gcg.com), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is determined using the algorithm of E. Myers and W. Miller (CABIOS, 4:11-17 (1989)) which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.

The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against sequence databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, et al. (J. Mol. Biol. 215:403-10 (1990)). BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to the nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to the proteins of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (Nucleic Acids Res. 25(17):3389-3402 (1997)). When utilizing BLAST and gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used.

Full-length pre-processed forms, as well as mature processed forms, of proteins that comprise one of the peptides of the present invention can readily be identified as having complete sequence identity to one of the transporter peptides of the present invention as well as being encoded by the same genetic locus as the transporter peptide provided herein. The gene encoding the novel transporter protein of the present invention is located on a genome component that has been mapped to human chromosome 6 (as indicated in Figure 3), which is supported by multiple lines of evidence, such as STS and BAC map data.

Allelic variants of a transporter peptide can readily be identified as being a human protein having a high degree (significant) of sequence homology/identity to at least a portion of the transporter peptide as well as being encoded by the same genetic locus as the transporter peptide provided herein. Genetic locus can readily be determined based on the genomic

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information provided in Figure 3, such as the genomic sequence mapped to the reference human. The gene encoding the novel transporter protein of the present invention is located on a genome component that has been mapped to human chromosome 6 (as indicated in Figure 3), which is supported by multiple lines of evidence, such as STS and BAC map data. As used herein, two proteins (or a region of the proteins) have significant homology when the amino acid sequences are typically at least about 70-80%, 80-90%, and more typically at least about 90-95% or more homologous. A significantly homologous amino acid sequence, according to the present invention, will be encoded by a nucleic acid sequence that will hybridize to a transporter peptide encoding nucleic acid molecule under stringent conditions as more fully described below.

Figure 3 provides information on SNPs that have been identified in a gene encoding the transporter protein of the present invention. 94 SNP variants were found, including 10 indels (indicated by a "-") and 1SNPs in exons. SNPs, identified at different nucleotide positions in introns and regions 5' and 3' of the ORF, may affect control/regulatory elements.

Paralogs of a transporter peptide can readily be identified as having some degree of significant sequence homology/identity to at least a portion of the transporter peptide, as being encoded by a gene from humans, and as having similar activity or function. Two proteins will typically be considered paralogs when the amino acid sequences are typically at least about 60% or greater, and more typically at least about 70% or greater homology through a given region or domain. Such paralogs will be encoded by a nucleic acid sequence that will hybridize to a transporter peptide encoding nucleic acid molecule under moderate to stringent conditions as more fully described below.

Orthologs of a transporter peptide can readily be identified as having some degree of significant sequence homology/identity to at least a portion of the transporter peptide as well as being encoded by a gene from another organism. Preferred orthologs will be isolated from mammals, preferably primates, for the development of human therapeutic targets and agents. Such orthologs will be encoded by a nucleic acid sequence that will hybridize to a transporter peptide encoding nucleic acid molecule under moderate to stringent conditions, as more fully described below, depending on the degree of relatedness of the two organisms yielding the proteins.

Non-naturally occurring variants of the transporter peptides of the present invention can readily be generated using recombinant techniques. Such variants include, but are not limited to

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deletions, additions and substitutions in the amino acid sequence of the transporter peptide. For example, one class of substitutions are conserved amino acid substitution. Such substitutions are those that substitute a given amino acid in a transporter peptide by another amino acid of like characteristics. Typically seen as conservative substitutions are the replacements, one for another, among the aliphatic amino acids Ala, Val, Leu, and Ile; interchange of the hydroxyl residues Ser and Thr; exchange of the acidic residues Asp and Glu; substitution between the amide residues Asn and Gln; exchange of the basic residues Lys and Arg; and replacements among the aromatic residues Phe and Tyr. Guidance concerning which amino acid changes are likely to be phenotypically silent are found in Bowie et al., Science 247:1306-1310 (1990).

Variant transporter peptides can be fully functional or can lack function in one or more activities, e.g. ability to bind ligand, ability to transport ligand, ability to mediate signaling, etc. Fully functional variants typically contain only conservative variation or variation in non-critical residues or in non-critical regions. Figure 2 provides the result of protein analysis and can be used to identify critical domains/regions. Functional variants can also contain substitution of similar amino acids that result in no change or an insignificant change in function. Alternatively, such substitutions may positively or negatively affect function to some degree.

Non-functional variants typically contain one or more non-conservative amino acid substitutions, deletions, insertions, inversions, or truncation or a substitution, insertion, inversion, or deletion in a critical residue or critical region.

Amino acids that are essential for function can be identified by methods known in the art, such as site-directed mutagenesis or alanine-scanning mutagenesis (Cunningham et al., Science 244:1081-1085 (1989)), particularly using the results provided in Figure 2. The latter procedure introduces single alanine mutations at every residue in the molecule. The resulting mutant molecules are then tested for biological activity such as transporter activity or in assays such as an in vitro proliferative activity. Sites that are critical for binding partner/substrate binding can also be determined by structural analysis such as crystallization, nuclear magnetic resonance or photoaffinity labeling (Smith et al., J. Mol. Biol. 224:899-904 (1992); de Vos et al. Science 255:306-312 (1992)).

The present invention further provides fragments of the transporter peptides, in addition to proteins and peptides that comprise and consist of such fragments, particularly those comprising the residues identified in Figure 2. The fragments to which the invention pertains,

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however, are not to be construed as encompassing fragments that may be disclosed publicly prior to the present invention.

As used herein, a fragment comprises at least 8, 10, 12, 14, 16, or more contiguous amino acid residues from a transporter peptide. Such fragments can be chosen based on the ability to retain one or more of the biological activities of the transporter peptide or could be chosen for the ability to perform a function, e.g. bind a substrate or act as an immunogen. Particularly important fragments are biologically active fragments, peptides that are, for example, about 8 or more amino acids in length. Such fragments will typically comprise a domain or motif of the transporter peptide, e.g., active site, a transmembrane domain or a substrate-binding domain. Further, possible fragments include, but are not limited to, domain or motif containing fragments, soluble peptide fragments, and fragments containing immunogenic structures. Predicted domains and functional sites are readily identifiable by computer programs well known and readily available to those of skill in the art (e.g., PROSITE analysis). The results of one such analysis are provided in Figure 2.

Polypeptides often contain amino acids other than the 20 amino acids commonly referred to as the 20 naturally occurring amino acids. Further, many amino acids, including the terminal amino acids, may be modified by natural processes, such as processing and other post-translational modifications, or by chemical modification techniques well known in the art. Common modifications that occur naturally in transporter peptides are described in basic texts, detailed monographs, and the research literature, and they are well known to those of skill in the art (some of these features are identified in Figure 2).

Known modifications include, but are not limited to, acetylation, acylation, ADPribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety,
covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or
lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization,
disulfide bond formation, demethylation, formation of covalent crosslinks, formation of cystine,
formation of pyroglutamate, formylation, gamma carboxylation, glycosylation, GPI anchor
formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic
processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA
mediated addition of amino acids to proteins such as arginylation, and ubiquitination.

Such modifications are well known to those of skill in the art and have been described in great detail in the scientific literature. Several particularly common modifications, glycosylation, lipid attachment, sulfation, gamma-carboxylation of glutamic acid residues,

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hydroxylation and ADP-ribosylation, for instance, are described in most basic texts, such as Proteins - Structure and Molecular Properties, 2nd Ed., T.E. Creighton, W. H. Freeman and Company, New York (1993). Many detailed reviews are available on this subject, such as by Wold, F., Posttranslational Covalent Modification of Proteins, B.C. Johnson, Ed., Academic Press, New York 1-12 (1983); Seifter et al. (Meth. Enzymol. 182: 626-646 (1990)) and Rattan et al. (Ann. N.Y. Acad. Sci. 663:48-62 (1992)).

Accordingly, the transporter peptides of the present invention also encompass derivatives or analogs in which a substituted amino acid residue is not one encoded by the genetic code, in which a substituent group is included, in which the mature transporter peptide is fused with another compound, such as a compound to increase the half-life of the transporter peptide (for example, polyethylene glycol), or in which the additional amino acids are fused to the mature transporter peptide, such as a leader or secretory sequence or a sequence for purification of the mature transporter peptide or a pro-protein sequence.

Protein/Peptide Uses

The proteins of the present invention can be used in substantial and specific assays related to the functional information provided in the Figures; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its binding partner or ligand) in biological fluids; and as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state). Where the protein binds or potentially binds to another protein or ligand (such as, for example, in a transporter-effector protein interaction or transporter-ligand interaction), the protein can be used to identify the binding partner/ligand so as to develop a system to identify inhibitors of the binding interaction. Any or all of these uses are capable of being developed into reagent grade or kit format for commercialization as commercial products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E. F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S. L. and A. R. Kimmel eds., 1987.

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The potential uses of the peptides of the present invention are based primarily on the source of the protein as well as the class/action of the protein. For example, transporters isolated from humans and their human/mammalian orthologs serve as targets for identifying agents for use in mammalian therapeutic applications, e.g. a human drug, particularly in modulating a biological or pathological response in a cell or tissue that expresses the transporter. Experimental data as provided in Figure 1 indicates that transporter proteins of the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas. Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans. A large percentage of pharmaceutical agents are being developed that modulate the activity of transporter proteins, particularly members of the Na+-independent transporter subfamily (see Background of the Invention). The structural and functional information provided in the Background and Figures provide specific and substantial uses for the molecules of the present invention, particularly in combination with the expression information provided in Figure 1. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. Such uses can readily be determined using the information provided herein, that known in the art and routine experimentation.

The proteins of the present invention (including variants and fragments that may have been disclosed prior to the present invention) are useful for biological assays related to transporters that are related to members of the Na+-independent transporter subfamily. Such assays involve any of the known transporter functions or activities or properties useful for diagnosis and treatment of transporter-related conditions that are specific for the subfamily of transporters that the one of the present invention belongs to, particularly in cells and tissues that express the transporter. Experimental data as provided in Figure 1 indicates that transporter proteins of the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas. Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans. The proteins of the present invention are also useful in drug screening assays, in cell-based or cell-free systems ((Hodgson, Bio/technology, 1992, Sept 10(9);973-80). Cell-based systems can be native, i.e., cells that normally express the transporter, as a biopsy or expanded in cell culture.

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Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. In an alternate embodiment, cell-based assays involve recombinant host cells expressing the transporter protein.

The polypeptides can be used to identify compounds that modulate transporter activity of the protein in its natural state or an altered form that causes a specific disease or pathology associated with the transporter. Both the transporters of the present invention and appropriate variants and fragments can be used in high-throughput screens to assay candidate compounds for the ability to bind to the transporter. These compounds can be further screened against a functional transporter to determine the effect of the compound on the transporter activity. Further, these compounds can be tested in animal or invertebrate systems to determine activity/effectiveness. Compounds can be identified that activate (agonist) or inactivate (antagonist) the transporter to a desired degree.

Further, the proteins of the present invention can be used to screen a compound for the ability to stimulate or inhibit interaction between the transporter protein and a molecule that normally interacts with the transporter protein, e.g. a substrate or a component of the signal pathway that the transporter protein normally interacts (for example, another transporter). Such assays typically include the steps of combining the transporter protein with a candidate compound under conditions that allow the transporter protein, or fragment, to interact with the target molecule, and to detect the formation of a complex between the protein and the target or to detect the biochemical consequence of the interaction with the transporter protein and the target, such as any of the associated effects of signal transduction such as changes in membrane potential, protein phosphorylation, cAMP turnover, and adenylate cyclase activation, etc.

Candidate compounds include, for example, 1) peptides such as soluble peptides, including Ig-tailed fusion peptides and members of random peptide libraries (see, e.g., Lam et al., Nature 354:82-84 (1991); Houghten et al., Nature 354:84-86 (1991)) and combinatorial chemistry-derived molecular libraries made of D- and/or L- configuration amino acids; 2) phosphopeptides (e.g., members of random and partially degenerate, directed phosphopeptide libraries, see, e.g., Songyang et al., Cell 72:767-778 (1993)); 3) antibodies (e.g., polyclonal, monoclonal, humanized, anti-idiotypic, chimeric, and single chain antibodies as well as Fab, F(ab')₂, Fab expression library fragments, and epitope-binding fragments of antibodies); and 4) small organic and inorganic molecules (e.g., molecules obtained from combinatorial and natural product libraries).

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One candidate compound is a soluble fragment of the receptor that competes for ligand binding. Other candidate compounds include mutant transporters or appropriate fragments containing mutations that affect transporter function and thus compete for ligand. Accordingly, a fragment that competes for ligand, for example with a higher affinity, or a fragment that binds ligand but does not allow release, is encompassed by the invention.

The invention further includes other end point assays to identify compounds that modulate (stimulate or inhibit) transporter activity. The assays typically involve an assay of events in the signal transduction pathway that indicate transporter activity. Thus, the transport of a ligand, change in cell membrane potential, activation of a protein, a change in the expression of genes that are up- or down-regulated in response to the transporter protein dependent signal cascade can be assayed.

Any of the biological or biochemical functions mediated by the transporter can be used as an endpoint assay. These include all of the biochemical or biochemical/biological events described herein, in the references cited herein, incorporated by reference for these endpoint assay targets, and other functions known to those of ordinary skill in the art or that can be readily identified using the information provided in the Figures, particularly Figure 2. Specifically, a biological function of a cell or tissues that expresses the transporter can be assayed. Experimental data as provided in Figure 1 indicates that transporter proteins of the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas. Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans.

Binding and/or activating compounds can also be screened by using chimeric transporter proteins in which the amino terminal extracellular domain, or parts thereof, the entire transmembrane domain or subregions, such as any of the seven transmembrane segments or any of the intracellular or extracellular loops and the carboxy terminal intracellular domain, or parts thereof, can be replaced by heterologous domains or subregions. For example, a ligand-binding region can be used that interacts with a different ligand then that which is recognized by the native transporter. Accordingly, a different set of signal transduction components is available as an end-point assay for activation. This allows for assays to be performed in other than the specific host cell from which the transporter is derived.

The proteins of the present invention are also useful in competition binding assays in methods designed to discover compounds that interact with the transporter (e.g. binding

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partners and/or ligands). Thus, a compound is exposed to a transporter polypeptide under conditions that allow the compound to bind or to otherwise interact with the polypeptide. Soluble transporter polypeptide is also added to the mixture. If the test compound interacts with the soluble transporter polypeptide, it decreases the amount of complex formed or activity from the transporter target. This type of assay is particularly useful in cases in which compounds are sought that interact with specific regions of the transporter. Thus, the soluble polypeptide that competes with the target transporter region is designed to contain peptide sequences corresponding to the region of interest.

To perform cell free drug screening assays, it is sometimes desirable to immobilize either the transporter protein, or fragment, or its target molecule to facilitate separation of complexes from uncomplexed forms of one or both of the proteins, as well as to accommodate automation of the assay.

Techniques for immobilizing proteins on matrices can be used in the drug screening assays. In one embodiment, a fusion protein can be provided which adds a domain that allows the protein to be bound to a matrix. For example, glutathione-S-transferase fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical, St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined with the cell lysates (e.g., ³⁵S-labeled) and the candidate compound, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads are washed to remove any unbound label, and the matrix immobilized and radiolabel determined directly, or in the supernatant after the complexes are dissociated. Alternatively, the complexes can be dissociated from the matrix, separated by SDS-PAGE, and the level of transporter-binding protein found in the bead fraction quantitated from the gel using standard electrophoretic techniques. For example, either the polypeptide or its target molecule can be immobilized utilizing conjugation of biotin and streptavidin using techniques well known in the art. Alternatively, antibodies reactive with the protein but which do not interfere with binding of the protein to its target molecule can be derivatized to the wells of the plate, and the protein trapped in the wells by antibody conjugation. Preparations of a transporter-binding protein and a candidate compound are incubated in the transporter protein-presenting wells and the amount of complex trapped in the well can be quantitated. Methods for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the transporter protein target molecule, or which are reactive with transporter protein and compete with the target molecule,

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as well as enzyme-linked assays which rely on detecting an enzymatic activity associated with the target molecule.

Agents that modulate one of the transporters of the present invention can be identified using one or more of the above assays, alone or in combination. It is generally preferable to use a cell-based or cell free system first and then confirm activity in an animal or other model system. Such model systems are well known in the art and can readily be employed in this context.

Modulators of transporter protein activity identified according to these drug screening assays can be used to treat a subject with a disorder mediated by the transporter pathway, by treating cells or tissues that express the transporter. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. These methods of treatment include the steps of administering a modulator of transporter activity in a pharmaceutical composition to a subject in need of such treatment, the modulator being identified as described herein.

In yet another aspect of the invention, the transporter proteins can be used as "bait proteins" in a two-hybrid assay or three-hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al. (1993) Cell 72:223-232; Madura et al. (1993) J. Biol. Chem. 268:12046-12054; Bartel et al. (1993) Biotechniques 14:920-924; Iwabuchi et al. (1993) Oncogene 8:1693-1696; and Brent WO94/10300), to identify other proteins, which bind to or interact with the transporter and are involved in transporter activity. Such transporter-binding proteins are also likely to be involved in the propagation of signals by the transporter proteins or transporter targets as, for example, downstream elements of a transporter-mediated signaling pathway. Alternatively, such transporter-binding proteins are likely to be transporter inhibitors.

The two-hybrid system is based on the modular nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for a transporter protein is fused to a gene encoding the DNA binding domain of a known transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If the "bait" and the "prey" proteins are able to interact, *in vivo*, forming a transporter-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This

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proximity allows transcription of a reporter gene (e.g., LacZ) which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes the protein which interacts with the transporter protein.

This invention further pertains to novel agents identified by the above-described screening assays. Accordingly, it is within the scope of this invention to further use an agent identified as described herein in an appropriate animal model. For example, an agent identified as described herein (e.g., a transporter-modulating agent, an antisense transporter nucleic acid molecule, a transporter-specific antibody, or a transporter-binding partner) can be used in an animal or other model to determine the efficacy, toxicity, or side effects of treatment with such an agent. Alternatively, an agent identified as described herein can be used in an animal or other model to determine the mechanism of action of such an agent. Furthermore, this invention pertains to uses of novel agents identified by the above-described screening assays for treatments as described herein.

The transporter proteins of the present invention are also useful to provide a target for diagnosing a disease or predisposition to disease mediated by the peptide. Accordingly, the invention provides methods for detecting the presence, or levels of, the protein (or encoding mRNA) in a cell, tissue, or organism. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. The method involves contacting a biological sample with a compound capable of interacting with the transporter protein such that the interaction can be detected. Such an assay can be provided in a single detection format or a multi-detection format such as an antibody chip array.

One agent for detecting a protein in a sample is an antibody capable of selectively binding to protein. A biological sample includes tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject.

The peptides of the present invention also provide targets for diagnosing active protein activity, disease, or predisposition to disease, in a patient having a variant peptide, particularly activities and conditions that are known for other members of the family of proteins to which the present one belongs. Thus, the peptide can be isolated from a biological sample and assayed for the presence of a genetic mutation that results in aberrant peptide. This includes amino acid substitution, deletion, insertion, rearrangement, (as the result of aberrant splicing events), and

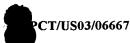
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inappropriate post-translational modification. Analytic methods include altered electrophoretic mobility, altered tryptic peptide digest, altered transporter activity in cell-based or cell-free assay, alteration in ligand or antibody-binding pattern, altered isoelectric point, direct amino acid sequencing, and any other of the known assay techniques useful for detecting mutations in a protein. Such an assay can be provided in a single detection format or a multi-detection format such as an antibody chip array.

In vitro techniques for detection of peptide include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence using a detection reagent, such as an antibody or protein binding agent. Alternatively, the peptide can be detected in vivo in a subject by introducing into the subject a labeled anti-peptide antibody or other types of detection agent. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques. Particularly useful are methods that detect the allelic variant of a peptide expressed in a subject and methods which detect fragments of a peptide in a sample.

The peptides are also useful in pharmacogenomic analysis. Pharmacogenomics deal with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Eichelbaum, M. (Clin. Exp. Pharmacol. Physiol. 23(10-11):983-985 (1996)), and Linder, M.W. (Clin. Chem. 43(2):254-266 (1997)). The clinical outcomes of these variations result in severe toxicity of therapeutic drugs in certain individuals or therapeutic failure of drugs in certain individuals as a result of individual variation in metabolism. Thus, the genotype of the individual can determine the way a therapeutic compound acts on the body or the way the body metabolizes the compound. Further, the activity of drug metabolizing enzymes effects both the intensity and duration of drug action. Thus, the pharmacogenomics of the individual permit the selection of effective compounds and effective dosages of such compounds for prophylactic or therapeutic treatment based on the individual's genotype. The discovery of genetic polymorphisms in some drug metabolizing enzymes has explained why some patients do not obtain the expected drug effects, show an exaggerated drug effect, or experience serious toxicity from standard drug dosages. Polymorphisms can be expressed in the phenotype of the extensive metabolizer and the phenotype of the poor metabolizer. Accordingly, genetic polymorphism may lead to allelic protein variants of the transporter protein in which one or more of the transporter functions in one population is different from those in another population. The peptides thus allow a target to ascertain a genetic predisposition that can affect treatment modality. Thus, in a ligand-based

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treatment, polymorphism may give rise to amino terminal extracellular domains and/or other ligand-binding regions that are more or less active in ligand binding, and transporter activation. Accordingly, ligand dosage would necessarily be modified to maximize the therapeutic effect within a given population containing a polymorphism. As an alternative to genotyping, specific polymorphic peptides could be identified.

The peptides are also useful for treating a disorder characterized by an absence of, inappropriate, or unwanted expression of the protein. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. Accordingly, methods for treatment include the use of the transporter protein or fragments.

Antibodies

The invention also provides antibodies that selectively bind to one of the peptides of the present invention, a protein comprising such a peptide, as well as variants and fragments thereof. As used herein, an antibody selectively binds a target peptide when it binds the target peptide and does not significantly bind to unrelated proteins. An antibody is still considered to selectively bind a peptide even if it also binds to other proteins that are not substantially homologous with the target peptide so long as such proteins share homology with a fragment or domain of the peptide target of the antibody. In this case, it would be understood that antibody binding to the peptide is still selective despite some degree of cross-reactivity.

As used herein, an antibody is defined in terms consistent with that recognized within the art: they are multi-subunit proteins produced by a mammalian organism in response to an antigen challenge. The antibodies of the present invention include polyclonal antibodies and monoclonal antibodies, as well as fragments of such antibodies, including, but not limited to, Fab or F(ab')₂, and Fv fragments.

Many methods are known for generating and/or identifying antibodies to a given target peptide. Several such methods are described by Harlow, Antibodies, Cold Spring Harbor Press, (1989).

In general, to generate antibodies, an isolated peptide is used as an immunogen and is administered to a mammalian organism, such as a rat, rabbit or mouse. The full-length protein, an antigenic peptide fragment or a fusion protein can be used. Particularly important fragments are those covering functional domains, such as the domains identified in Figure 2, and domain

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of sequence homology or divergence amongst the family, such as those that can readily be identified using protein alignment methods and as presented in the Figures.

Antibodies are preferably prepared from regions or discrete fragments of the transporter proteins. Antibodies can be prepared from any region of the peptide as described herein. However, preferred regions will include those involved in function/activity and/or transporter/binding partner interaction. Figure 2 can be used to identify particularly important regions while sequence alignment can be used to identify conserved and unique sequence fragments.

An antigenic fragment will typically comprise at least 8 contiguous amino acid residues. The antigenic peptide can comprise, however, at least 10, 12, 14, 16 or more amino acid residues. Such fragments can be selected on a physical property, such as fragments correspond to regions that are located on the surface of the protein, e.g., hydrophilic regions or can be selected based on sequence uniqueness (see Figure 2).

Detection on an antibody of the present invention can be facilitated by coupling (i.e., physically linking) the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ¹²⁵I, ¹³¹I, ³⁵S or ³H.

Antibody Uses

The antibodies can be used to isolate one of the proteins of the present invention by standard techniques, such as affinity chromatography or immunoprecipitation. The antibodies can facilitate the purification of the natural protein from cells and recombinantly produced protein expressed in host cells. In addition, such antibodies are useful to detect the presence of one of the proteins of the present invention in cells or tissues to determine the pattern of expression of the protein among various tissues in an organism and over the course of normal development. Experimental data as provided in Figure 1 indicates that transporter proteins of

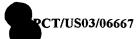
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the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas. Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans. Further, such antibodies can be used to detect protein *in situ*, *in vitro*, or in a cell lysate or supernatant in order to evaluate the abundance and pattern of expression. Also, such antibodies can be used to assess abnormal tissue distribution or abnormal expression during development or progression of a biological condition. Antibody detection of circulating fragments of the full length protein can be used to identify turnover.

Further, the antibodies can be used to assess expression in disease states such as in active stages of the disease or in an individual with a predisposition toward disease related to the protein's function. When a disorder is caused by an inappropriate tissue distribution, developmental expression, level of expression of the protein, or expressed/processed form, the antibody can be prepared against the normal protein. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. If a disorder is characterized by a specific mutation in the protein, antibodies specific for this mutant protein can be used to assay for the presence of the specific mutant protein.

The antibodies can also be used to assess normal and aberrant subcellular localization of cells in the various tissues in an organism. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. The diagnostic uses can be applied, not only in genetic testing, but also in monitoring a treatment modality. Accordingly, where treatment is ultimately aimed at correcting expression level or the presence of aberrant sequence and aberrant tissue distribution or developmental expression, antibodies directed against the protein or relevant fragments can be used to monitor therapeutic efficacy.

Additionally, antibodies are useful in pharmacogenomic analysis. Thus, antibodies prepared against polymorphic proteins can be used to identify individuals that require modified treatment modalities. The antibodies are also useful as diagnostic tools as an immunological marker for aberrant protein analyzed by electrophoretic mobility, isoelectric point, tryptic peptide digest, and other physical assays known to those in the art.

The antibodies are also useful for tissue typing. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as

well as in different tissues. Thus, where a specific protein has been correlated with expression in a specific tissue, antibodies that are specific for this protein can be used to identify a tissue type.

The antibodies are also useful for inhibiting protein function, for example, blocking the binding of the transporter peptide to a binding partner such as a ligand or protein binding partner. These uses can also be applied in a therapeutic context in which treatment involves inhibiting the protein's function. An antibody can be used, for example, to block binding, thus modulating (agonizing or antagonizing) the peptides activity. Antibodies can be prepared against specific fragments containing sites required for function or against intact protein that is associated with a cell or cell membrane. See Figure 2 for structural information relating to the proteins of the present invention.

The invention also encompasses kits for using antibodies to detect the presence of a protein in a biological sample. The kit can comprise antibodies such as a labeled or labelable antibody and a compound or agent for detecting protein in a biological sample; means for determining the amount of protein in the sample; means for comparing the amount of protein in the sample with a standard; and instructions for use. Such a kit can be supplied to detect a single protein or epitope or can be configured to detect one of a multitude of epitopes, such as in an antibody detection array. Arrays are described in detail below for nucleic acid arrays and similar methods have been developed for antibody arrays.

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Nucleic Acid Molecules

The present invention further provides isolated nucleic acid molecules that encode a transporter peptide or protein of the present invention (cDNA, transcript and genomic sequence). Such nucleic acid molecules will consist of, consist essentially of, or comprise a nucleotide sequence that encodes one of the transporter peptides of the present invention, an allelic variant thereof, or an ortholog or paralog thereof.

As used herein, an "isolated" nucleic acid molecule is one that is separated from other nucleic acid present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences that naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. However, there can be some flanking nucleotide sequences, for example up to about 5KB, 4KB, 3KB, 2KB, or 1KB or less, particularly contiguous peptide encoding sequences and peptide encoding sequences within the same gene but separated by introns in the

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genomic sequence. The important point is that the nucleic acid is isolated from remote and unimportant flanking sequences such that it can be subjected to the specific manipulations described herein such as recombinant expression, preparation of probes and primers, and other uses specific to the nucleic acid sequences.

Moreover, an "isolated" nucleic acid molecule, such as a transcript/cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or chemical precursors or other chemicals when chemically synthesized. However, the nucleic acid molecule can be fused to other coding or regulatory sequences and still be considered isolated.

For example, recombinant DNA molecules contained in a vector are considered isolated. Further examples of isolated DNA molecules include recombinant DNA molecules maintained in heterologous host cells or purified (partially or substantially) DNA molecules in solution. Isolated RNA molecules include *in vivo* or *in vitro* RNA transcripts of the isolated DNA molecules of the present invention. Isolated nucleic acid molecules according to the present invention further include such molecules produced synthetically.

Accordingly, the present invention provides nucleic acid molecules that consist of the nucleotide sequence shown in Figure 1 or 3 (SEQ ID NO:1, transcript sequence and SEQ ID NO:3, genomic sequence), or any nucleic acid molecule that encodes the protein provided in Figure 2, SEQ ID NO:2. A nucleic acid molecule consists of a nucleotide sequence when the nucleotide sequence is the complete nucleotide sequence of the nucleic acid molecule.

The present invention further provides nucleic acid molecules that consist essentially of the nucleotide sequence shown in Figure 1 or 3 (SEQ ID NO:1, transcript sequence and SEQ ID NO:3, genomic sequence), or any nucleic acid molecule that encodes the protein provided in Figure 2, SEQ ID NO:2. A nucleic acid molecule consists essentially of a nucleotide sequence when such a nucleotide sequence is present with only a few additional nucleic acid residues in the final nucleic acid molecule.

The present invention further provides nucleic acid molecules that comprise the nucleotide sequences shown in Figure 1 or 3 (SEQ ID NO:1, transcript sequence and SEQ ID NO:3, genomic sequence), or any nucleic acid molecule that encodes the protein provided in Figure 2, SEQ ID NO:2. A nucleic acid molecule comprises a nucleotide sequence when the nucleotide sequence is at least part of the final nucleotide sequence of the nucleic acid molecule. In such a fashion, the nucleic acid molecule can be only the nucleotide sequence or have additional nucleic acid residues, such as nucleic acid residues that are naturally associated with

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it or heterologous nucleotide sequences. Such a nucleic acid molecule can have a few additional nucleotides or can comprise several hundred or more additional nucleotides. A brief description of how various types of these nucleic acid molecules can be readily made/isolated is provided below.

In Figures 1 and 3, both coding and non-coding sequences are provided. Because of the source of the present invention, humans genomic sequence (Figure 3) and cDNA/transcript sequences (Figure 1), the nucleic acid molecules in the Figures will contain genomic intronic sequences, 5' and 3' non-coding sequences, gene regulatory regions and non-coding intergenic sequences. In general such sequence features are either noted in Figures 1 and 3 or can readily be identified using computational tools known in the art. As discussed below, some of the non-coding regions, particularly gene regulatory elements such as promoters, are useful for a variety of purposes, e.g. control of heterologous gene expression, target for identifying gene activity modulating compounds, and are particularly claimed as fragments of the genomic sequence provided herein.

The isolated nucleic acid molecules can encode the mature protein plus additional amino or carboxyl-terminal amino acids, or amino acids interior to the mature peptide (when the mature form has more than one peptide chain, for instance). Such sequences may play a role in processing of a protein from precursor to a mature form, facilitate protein trafficking, prolong or shorten protein half-life or facilitate manipulation of a protein for assay or production, among other things. As generally is the case *in situ*, the additional amino acids may be processed away from the mature protein by cellular enzymes.

As mentioned above, the isolated nucleic acid molecules include, but are not limited to, the sequence encoding the transporter peptide alone, the sequence encoding the mature peptide and additional coding sequences, such as a leader or secretory sequence (e.g., a pre-pro or proprotein sequence), the sequence encoding the mature peptide, with or without the additional coding sequences, plus additional non-coding sequences, for example introns and non-coding 5' and 3' sequences such as transcribed but non-translated sequences that play a role in transcription, mRNA processing (including splicing and polyadenylation signals), ribosome binding and stability of mRNA. In addition, the nucleic acid molecule may be fused to a marker sequence encoding, for example, a peptide that facilitates purification.

Isolated nucleic acid molecules can be in the form of RNA, such as mRNA, or in the form DNA, including cDNA and genomic DNA obtained by cloning or produced by chemical synthetic techniques or by a combination thereof. The nucleic acid, especially DNA, can be

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double-stranded or single-stranded. Single-stranded nucleic acid can be the coding strand (sense strand) or the non-coding strand (anti-sense strand).

The invention further provides nucleic acid molecules that encode fragments of the peptides of the present invention as well as nucleic acid molecules that encode obvious variants of the transporter proteins of the present invention that are described above. Such nucleic acid molecules may be naturally occurring, such as allelic variants (same locus), paralogs (different locus), and orthologs (different organism), or may be constructed by recombinant DNA methods or by chemical synthesis. Such non-naturally occurring variants may be made by mutagenesis techniques, including those applied to nucleic acid molecules, cells, or organisms. Accordingly, as discussed above, the variants can contain nucleotide substitutions, deletions, inversions and insertions. Variation can occur in either or both the coding and non-coding regions. The variations can produce both conservative and non-conservative amino acid substitutions.

The present invention further provides non-coding fragments of the nucleic acid molecules provided in Figures 1 and 3. Preferred non-coding fragments include, but are not limited to, promoter sequences, enhancer sequences, gene modulating sequences and gene termination sequences. Such fragments are useful in controlling heterologous gene expression and in developing screens to identify gene-modulating agents. A promoter can readily be identified as being 5' to the ATG start site in the genomic sequence provided in Figure 3.

A fragment comprises a contiguous nucleotide sequence greater than 12 or more nucleotides. Further, a fragment could at least 30, 40, 50, 100, 250 or 500 nucleotides in length. The length of the fragment will be based on its intended use. For example, the fragment can encode epitope bearing regions of the peptide, or can be useful as DNA probes and primers. Such fragments can be isolated using the known nucleotide sequence to synthesize an oligonucleotide probe. A labeled probe can then be used to screen a cDNA library, genomic DNA library, or mRNA to isolate nucleic acid corresponding to the coding region. Further, primers can be used in PCR reactions to clone specific regions of gene.

A probe/primer typically comprises substantially a purified oligonucleotide or oligonucleotide pair. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, 20, 25, 40, 50 or more consecutive nucleotides.

Orthologs, homologs, and allelic variants can be identified using methods well known in the art. As described in the Peptide Section, these variants comprise a nucleotide sequence

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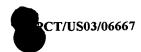
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encoding a peptide that is typically 60-70%, 70-80%, 80-90%, and more typically at least about 90-95% or more homologous to the nucleotide sequence shown in the Figure sheets or a fragment of this sequence. Such nucleic acid molecules can readily be identified as being able to hybridize under moderate to stringent conditions, to the nucleotide sequence shown in the Figure sheets or a fragment of the sequence. Allelic variants can readily be determined by genetic locus of the encoding gene. The gene encoding the novel transporter protein of the present invention is located on a genome component that has been mapped to human chromosome 6 (as indicated in Figure 3), which is supported by multiple lines of evidence, such as STS and BAC map data.

Figure 3 provides information on SNPs that have been identified in a gene encoding the transporter protein of the present invention. 94 SNP variants were found, including 10 indels (indicated by a "-") and 1SNPs in exons. SNPs, identified at different nucleotide positions in introns and regions 5' and 3' of the ORF, may affect control/regulatory elements.

As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences encoding a peptide at least 60-70% homologous to each other typically remain hybridized to each other. The conditions can be such that sequences at least about 60%, at least about 70%, or at least about 80% or more homologous to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. One example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45C, followed by one or more washes in 0.2 X SSC, 0.1% SDS at 50-65C. Examples of moderate to low stringency hybridization conditions are well known in the art.

Nucleic Acid Molecule Uses

The nucleic acid molecules of the present invention are useful for probes, primers, chemical intermediates, and in biological assays. The nucleic acid molecules are useful as a hybridization probe for messenger RNA, transcript/cDNA and genomic DNA to isolate full-length cDNA and genomic clones encoding the peptide described in Figure 2 and to isolate cDNA and genomic clones that correspond to variants (alleles, orthologs, etc.) producing the same or related peptides shown in Figure 2. 94 SNPs, including 10 indels, have been identified

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in the gene encoding the transporter protein provided by the present invention and are given in Figure 3.

The probe can correspond to any sequence along the entire length of the nucleic acid molecules provided in the Figures. Accordingly, it could be derived from 5' noncoding regions, the coding region, and 3' noncoding regions. However, as discussed, fragments are not to be construed as encompassing fragments disclosed prior to the present invention.

The nucleic acid molecules are also useful as primers for PCR to amplify any given region of a nucleic acid molecule and are useful to synthesize antisense molecules of desired length and sequence.

The nucleic acid molecules are also useful for constructing recombinant vectors. Such vectors include expression vectors that express a portion of, or all of, the peptide sequences. Vectors also include insertion vectors, used to integrate into another nucleic acid molecule sequence, such as into the cellular genome, to alter *in situ* expression of a gene and/or gene product. For example, an endogenous coding sequence can be replaced via homologous recombination with all or part of the coding region containing one or more specifically introduced mutations.

The nucleic acid molecules are also useful for expressing antigenic portions of the proteins.

The nucleic acid molecules are also useful as probes for determining the chromosomal positions of the nucleic acid molecules by means of *in situ* hybridization methods. The gene encoding the novel transporter protein of the present invention is located on a genome component that has been mapped to human chromosome 6 (as indicated in Figure 3), which is supported by multiple lines of evidence, such as STS and BAC map data.

The nucleic acid molecules are also useful in making vectors containing the gene regulatory regions of the nucleic acid molecules of the present invention.

The nucleic acid molecules are also useful for designing ribozymes corresponding to all, or a part, of the mRNA produced from the nucleic acid molecules described herein.

The nucleic acid molecules are also useful for making vectors that express part, or all, of the peptides.

The nucleic acid molecules are also useful for constructing host cells expressing a part, or all, of the nucleic acid molecules and peptides.

The nucleic acid molecules are also useful for constructing transgenic animals expressing all, or a part, of the nucleic acid molecules and peptides.

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The nucleic acid molecules are also useful as hybridization probes for determining the presence, level, form and distribution of nucleic acid expression. Experimental data as provided in Figure 1 indicates that transporter proteins of the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas.

Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans.

Accordingly, the probes can be used to detect the presence of, or to determine levels of, a specific nucleic acid molecule in cells, tissues, and in organisms. The nucleic acid whose level is determined can be DNA or RNA. Accordingly, probes corresponding to the peptides described herein can be used to assess expression and/or gene copy number in a given cell, tissue, or organism. These uses are relevant for diagnosis of disorders involving an increase or decrease in transporter protein expression relative to normal results.

In vitro techniques for detection of mRNA include Northern hybridizations and in situ hybridizations. In vitro techniques for detecting DNA include Southern hybridizations and in situ hybridization.

Probes can be used as a part of a diagnostic test kit for identifying cells or tissues that express a transporter protein, such as by measuring a level of a transporter-encoding nucleic acid in a sample of cells from a subject e.g., mRNA or genomic DNA, or determining if a transporter gene has been mutated. Experimental data as provided in Figure 1 indicates that transporter proteins of the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas. Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans.

Nucleic acid expression assays are useful for drug screening to identify compounds that modulate transporter nucleic acid expression.

The invention thus provides a method for identifying a compound that can be used to treat a disorder associated with nucleic acid expression of the transporter gene, particularly biological and pathological processes that are mediated by the transporter in cells and tissues that express it. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues. The method typically includes assaying the ability of the compound to modulate the expression of the transporter nucleic acid and thus identifying a compound that can be used to treat a disorder

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characterized by undesired transporter nucleic acid expression. The assays can be performed in cell-based and cell-free systems. Cell-based assays include cells naturally expressing the transporter nucleic acid or recombinant cells genetically engineered to express specific nucleic acid sequences.

The assay for transporter nucleic acid expression can involve direct assay of nucleic acid levels, such as mRNA levels, or on collateral compounds involved in the signal pathway. Further, the expression of genes that are up- or down-regulated in response to the transporter protein signal pathway can also be assayed. In this embodiment the regulatory regions of these genes can be operably linked to a reporter gene such as luciferase.

Thus, modulators of transporter gene expression can be identified in a method wherein a cell is contacted with a candidate compound and the expression of mRNA determined. The level of expression of transporter mRNA in the presence of the candidate compound is compared to the level of expression of transporter mRNA in the absence of the candidate compound. The candidate compound can then be identified as a modulator of nucleic acid expression based on this comparison and be used, for example to treat a disorder characterized by aberrant nucleic acid expression. When expression of mRNA is statistically significantly greater in the presence of the candidate compound than in its absence, the candidate compound is identified as a stimulator of nucleic acid expression. When nucleic acid expression is statistically significantly less in the presence of the candidate compound than in its absence, the candidate compound is identified as an inhibitor of nucleic acid expression.

The invention further provides methods of treatment, with the nucleic acid as a target, using a compound identified through drug screening as a gene modulator to modulate transporter nucleic acid expression in cells and tissues that express the transporter.

Experimental data as provided in Figure 1 indicates that transporter proteins of the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas. Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans. Modulation includes both up-regulation (i.e. activation or agonization) or down-regulation (suppression or antagonization) or nucleic acid expression.

Alternatively, a modulator for transporter nucleic acid expression can be a small molecule or drug identified using the screening assays described herein as long as the drug or small molecule inhibits the transporter nucleic acid expression in the cells and tissues that

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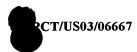
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express the protein. Experimental data as provided in Figure 1 indicates expression in humans in the organs such as lung, brain and prostate etc, as well as in different tissues.

The nucleic acid molecules are also useful for monitoring the effectiveness of modulating compounds on the expression or activity of the transporter gene in clinical trials or in a treatment regimen. Thus, the gene expression pattern can serve as a barometer for the continuing effectiveness of treatment with the compound, particularly with compounds to which a patient can develop resistance. The gene expression pattern can also serve as a marker indicative of a physiological response of the affected cells to the compound. Accordingly, such monitoring would allow either increased administration of the compound or the administration of alternative compounds to which the patient has not become resistant. Similarly, if the level of nucleic acid expression falls below a desirable level, administration of the compound could be commensurately decreased.

The nucleic acid molecules are also useful in diagnostic assays for qualitative changes in transporter nucleic acid expression, and particularly in qualitative changes that lead to pathology. The nucleic acid molecules can be used to detect mutations in transporter genes and gene expression products such as mRNA. The nucleic acid molecules can be used as hybridization probes to detect naturally occurring genetic mutations in the transporter gene and thereby to determine whether a subject with the mutation is at risk for a disorder caused by the mutation. Mutations include deletion, addition, or substitution of one or more nucleotides in the gene, chromosomal rearrangement, such as inversion or transposition, modification of genomic DNA, such as aberrant methylation patterns or changes in gene copy number, such as amplification. Detection of a mutated form of the transporter gene associated with a dysfunction provides a diagnostic tool for an active disease or susceptibility to disease when the disease results from overexpression, underexpression, or altered expression of a transporter protein.

Individuals carrying mutations in the transporter gene can be detected at the nucleic acid level by a variety of techniques. Figure 3 provides information on SNPs that have been identified in a gene encoding the transporter protein of the present invention. 94 SNP variants were found, including 10 indels (indicated by a "-") and 1 SNPs in exons. SNPs, identified at different nucleotide positions in introns and regions 5' and 3' of the ORF, may affect control/regulatory elements. The gene encoding the novel transporter protein of the present invention is located on a genome component that has been mapped to human chromosome 6 (as indicated in Figure 3), which is supported by multiple lines of evidence,

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such as STS and BAC map data. Genomic DNA can be analyzed directly or can be amplified by using PCR prior to analysis. RNA or cDNA can be used in the same way. In some uses, detection of the mutation involves the use of a probe/primer in a polymerase chain reaction (PCR) (see, e.g. U.S. Patent Nos. 4,683,195 and 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, e.g., Landegran et al., Science 241:1077-1080 (1988); and Nakazawa et al., PNAS 91:360-364 (1994)), the latter of which can be particularly useful for detecting point mutations in the gene (see Abravaya et al., Nucleic Acids Res. 23:675-682 (1995)). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a gene under conditions such that hybridization and amplification of the gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. Deletions and insertions can be detected by a change in size of the amplified product compared to the normal genotype. Point mutations can be identified by hybridizing amplified DNA to normal RNA or antisense DNA sequences.

Alternatively, mutations in a transporter gene can be directly identified, for example, by alterations in restriction enzyme digestion patterns determined by gel electrophoresis.

Further, sequence-specific ribozymes (U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site. Perfectly matched sequences can be distinguished from mismatched sequences by nuclease cleavage digestion assays or by differences in melting temperature.

Sequence changes at specific locations can also be assessed by nuclease protection assays such as RNase and S1 protection or the chemical cleavage method. Furthermore, sequence differences between a mutant transporter gene and a wild-type gene can be determined by direct DNA sequencing. A variety of automated sequencing procedures can be utilized when performing the diagnostic assays (Naeve, C.W., (1995) *Biotechniques 19*:448), including sequencing by mass spectrometry (see, e.g., PCT International Publication No. WO 94/16101; Cohen et al., Adv. Chromatogr. 36:127-162 (1996); and Griffin et al., Appl. Biochem. Biotechnol. 38:147-159 (1993)).

Other methods for detecting mutations in the gene include methods in which protection from cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA duplexes (Myers et al., Science 230:1242 (1985)); Cotton et al., PNAS 85:4397 (1988); Saleeba et al.,

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Meth. Enzymol. 217:286-295 (1992)), electrophoretic mobility of mutant and wild type nucleic acid is compared (Orita et al., PNAS 86:2766 (1989); Cotton et al., Mutat. Res. 285:125-144 (1993); and Hayashi et al., Genet. Anal. Tech. Appl. 9:73-79 (1992)), and movement of mutant or wild-type fragments in polyacrylamide gels containing a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (Myers et al., Nature 313:495 (1985)). Examples of other techniques for detecting point mutations include selective oligonucleotide hybridization, selective amplification, and selective primer extension.

The nucleic acid molecules are also useful for testing an individual for a genotype that while not necessarily causing the disease, nevertheless affects the treatment modality. Thus, the nucleic acid molecules can be used to study the relationship between an individual's genotype and the individual's response to a compound used for treatment (pharmacogenomic relationship). Accordingly, the nucleic acid molecules described herein can be used to assess the mutation content of the transporter gene in an individual in order to select an appropriate compound or dosage regimen for treatment. Figure 3 provides information on SNPs that have been identified in a gene encoding the transporter protein of the present invention. 94 SNP variants were found, including 10 indels (indicated by a "-") and 1SNPs in exons. SNPs, identified at different nucleotide positions in introns and regions 5' and 3' of the ORF, may affect control/regulatory elements.

Thus nucleic acid molecules displaying genetic variations that affect treatment provide a diagnostic target that can be used to tailor treatment in an individual. Accordingly, the production of recombinant cells and animals containing these polymorphisms allow effective clinical design of treatment compounds and dosage regimens.

The nucleic acid molecules are thus useful as antisense constructs to control transporter gene expression in cells, tissues, and organisms. A DNA antisense nucleic acid molecule is designed to be complementary to a region of the gene involved in transcription, preventing transcription and hence production of transporter protein. An antisense RNA or DNA nucleic acid molecule would hybridize to the mRNA and thus block translation of mRNA into transporter protein.

Alternatively, a class of antisense molecules can be used to inactivate mRNA in order to decrease expression of transporter nucleic acid. Accordingly, these molecules can treat a disorder characterized by abnormal or undesired transporter nucleic acid expression. This technique involves cleavage by means of ribozymes containing nucleotide sequences complementary to one or more regions in the mRNA that attenuate the ability of the mRNA to

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be translated. Possible regions include coding regions and particularly coding regions corresponding to the catalytic and other functional activities of the transporter protein, such as ligand binding.

The nucleic acid molecules also provide vectors for gene therapy in patients containing cells that are aberrant in transporter gene expression. Thus, recombinant cells, which include the patient's cells that have been engineered ex vivo and returned to the patient, are introduced into an individual where the cells produce the desired transporter protein to treat the individual.

The invention also encompasses kits for detecting the presence of a transporter nucleic acid in a biological sample. Experimental data as provided in Figure 1 indicates that transporter proteins of the present invention are expressed in the human lung, brain, prostate, ovary, placenta, thymus, colon, and pancreas. Specifically, the protein also expressed in the tissues such as small cell carcinoma, liver, neuroblastoma cells, pooled germ cell tumors, adenocarcinoma, fibrotheoma, pooled germ cell tumors and Islets of Langerhans. For example, the kit can comprise reagents such as a labeled or labelable nucleic acid or agent capable of detecting transporter nucleic acid in a biological sample; means for determining the amount of transporter nucleic acid in the sample; and means for comparing the amount of transporter nucleic acid in the sample with a standard. The compound or agent can be packaged in a suitable container. The kit can further comprise instructions for using the kit to detect transporter protein mRNA or DNA.

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Nucleic Acid Arrays

The present invention further provides nucleic acid detection kits, such as arrays or microarrays of nucleic acid molecules that are based on the sequence information provided in Figures 1 and 3 (SEQ ID NOS:1 and 3).

As used herein "Arrays" or "Microarrays" refers to an array of distinct polynucleotides or oligonucleotides synthesized on a substrate, such as paper, nylon or other type of membrane, filter, chip, glass slide, or any other suitable solid support. In one embodiment, the microarray is prepared and used according to the methods described in US Patent 5,837,832, Chee *et al.*, PCT application W095/11995 (Chee *et al.*), Lockhart, D. J. *et al.* (1996; Nat. Biotech. 14: 1675-1680) and Schena, M. *et al.* (1996; Proc. Natl. Acad. Sci. 93: 10614-10619), all of which are incorporated herein in their entirety by reference. In other embodiments, such arrays are produced by the methods described by Brown *et al.*, US Patent No. 5,807,522.



The microarray or detection kit is preferably composed of a large number of unique, single-stranded nucleic acid sequences, usually either synthetic antisense oligonucleotides or fragments of cDNAs, fixed to a solid support. The oligonucleotides are preferably about 6-60 nucleotides in length, more preferably 15-30 nucleotides in length, and most preferably about 20-25 nucleotides in length. For a certain type of microarray or detection kit, it may be preferable to use oligonucleotides that are only 7-20 nucleotides in length. The microarray or detection kit may contain oligonucleotides that cover the known 5', or 3', sequence, sequential oligonucleotides that cover the full length sequence; or unique oligonucleotides selected from particular areas along the length of the sequence. Polynucleotides used in the microarray or detection kit may be oligonucleotides that are specific to a gene or genes of interest.

In order to produce oligonucleotides to a known sequence for a microarray or detection kit, the gene(s) of interest (or an ORF identified from the contigs of the present invention) is typically examined using a computer algorithm which starts at the 5' or at the 3' end of the nucleotide sequence. Typical algorithms will then identify oligomers of defined length that are unique to the gene, have a GC content within a range suitable for hybridization, and lack predicted secondary structure that may interfere with hybridization. In certain situations it may be appropriate to use pairs of oligonucleotides on a microarray or detection kit. The "pairs" will be identical, except for one nucleotide that preferably is located in the center of the sequence. The second oligonucleotide in the pair (mismatched by one) serves as a control. The number of oligonucleotide pairs may range from two to one million. The oligomers are synthesized at designated areas on a substrate using a light-directed chemical process. The substrate may be paper, nylon or other type of membrane, filter, chip, glass slide or any other suitable solid support.

In another aspect, an oligonucleotide may be synthesized on the surface of the substrate by using a chemical coupling procedure and an ink jet application apparatus, as described in PCT application W095/251116 (Baldeschweiler *et al.*) which is incorporated herein in its entirety by reference. In another aspect, a "gridded" array analogous to a dot (or slot) blot may be used to arrange and link cDNA fragments or oligonucleotides to the surface of a substrate using a vacuum system, thermal, UV, mechanical or chemical bonding procedures. An array, such as those described above, may be produced by hand or by using available devices (slot blot or dot blot apparatus), materials (any suitable solid support), and machines (including robotic instruments), and may contain 8, 24, 96, 384, 1536, 6144 or

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more oligonucleotides, or any other number between two and one million which lends itself to the efficient use of commercially available instrumentation.

In order to conduct sample analysis using a microarray or detection kit, the RNA or DNA from a biological sample is made into hybridization probes. The mRNA is isolated, and cDNA is produced and used as a template to make antisense RNA (aRNA). The aRNA is amplified in the presence of fluorescent nucleotides, and labeled probes are incubated with the microarray or detection kit so that the probe sequences hybridize to complementary oligonucleotides of the microarray or detection kit. Incubation conditions are adjusted so that hybridization occurs with precise complementary matches or with various degrees of less complementarity. After removal of nonhybridized probes, a scanner is used to determine the levels and patterns of fluorescence. The scanned images are examined to determine degree of complementarity and the relative abundance of each oligonucleotide sequence on the microarray or detection kit. The biological samples may be obtained from any bodily fluids (such as blood, urine, saliva, phlegm, gastric juices, etc.), cultured cells, biopsies, or other tissue preparations. A detection system may be used to measure the absence, presence, and amount of hybridization for all of the distinct sequences simultaneously. This data may be used for large-scale correlation studies on the sequences, expression patterns, mutations, variants, or polymorphisms among samples.

Using such arrays, the present invention provides methods to identify the expression of the transporter proteins/peptides of the present invention. In detail, such methods comprise incubating a test sample with one or more nucleic acid molecules and assaying for binding of the nucleic acid molecule with components within the test sample. Such assays will typically involve arrays comprising many genes, at least one of which is a gene of the present invention and or alleles of the transporter gene of the present invention. Figure 3 provides information on SNPs that have been identified in a gene encoding the transporter protein of the present invention. 94 SNP variants were found, including 10 indels (indicated by a "-") and 1SNPs in exons. SNPs, identified at different nucleotide positions in introns and regions 5' and 3' of the ORF, may affect control/regulatory elements.

Conditions for incubating a nucleic acid molecule with a test sample vary.

Incubation conditions depend on the format employed in the assay, the detection methods employed, and the type and nature of the nucleic acid molecule used in the assay. One skilled in the art will recognize that any one of the commonly available hybridization, amplification or array assay formats can readily be adapted to employ the novel fragments of

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the Human genome disclosed herein. Examples of such assays can be found in Chard, T, An Introduction to Radioimmunoassay and Related Techniques, Elsevier Science Publishers, Amsterdam, The Netherlands (1986); Bullock, G. R. et al., Techniques in Immunocytochemistry, Academic Press, Orlando, FL Vol. 1 (1982), Vol. 2 (1983), Vol. 3 (1985); Tijssen, P., Practice and Theory of Enzyme Immunoassays: Laboratory Techniques in Biochemistry and Molecular Biology, Elsevier Science Publishers, Amsterdam, The Netherlands (1985).

The test samples of the present invention include cells, protein or membrane extracts of cells. The test sample used in the above-described method will vary based on the assay format, nature of the detection method and the tissues, cells or extracts used as the sample to be assayed. Methods for preparing nucleic acid extracts or of cells are well known in the art and can be readily be adapted in order to obtain a sample that is compatible with the system utilized.

In another embodiment of the present invention, kits are provided which contain the necessary reagents to carry out the assays of the present invention.

Specifically, the invention provides a compartmentalized kit to receive, in close confinement, one or more containers which comprises: (a) a first container comprising one of the nucleic acid molecules that can bind to a fragment of the Human genome disclosed herein; and (b) one or more other containers comprising one or more of the following: wash reagents, reagents capable of detecting presence of a bound nucleic acid.

In detail, a compartmentalized kit includes any kit in which reagents are contained in separate containers. Such containers include small glass containers, plastic containers, strips of plastic, glass or paper, or arraying material such as silica. Such containers allows one to efficiently transfer reagents from one compartment to another compartment such that the samples and reagents are not cross-contaminated, and the agents or solutions of each container can be added in a quantitative fashion from one compartment to another. Such containers will include a container which will accept the test sample, a container which contains the nucleic acid probe, containers which contain wash reagents (such as phosphate buffered saline, Tris-buffers, etc.), and containers which contain the reagents used to detect the bound probe. One skilled in the art will readily recognize that the previously unidentified transporter gene of the present invention can be routinely identified using the sequence information disclosed herein can be readily incorporated into one of the established kit formats which are well known in the art, particularly expression arrays.

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Vectors/host cells

The invention also provides vectors containing the nucleic acid molecules described herein. The term "vector" refers to a vehicle, preferably a nucleic acid molecule, which can transport the nucleic acid molecules. When the vector is a nucleic acid molecule, the nucleic acid molecules are covalently linked to the vector nucleic acid. With this aspect of the invention, the vector includes a plasmid, single or double stranded phage, a single or double stranded RNA or DNA viral vector, or artificial chromosome, such as a BAC, PAC, YAC, OR MAC.

A vector can be maintained in the host cell as an extrachromosomal element where it replicates and produces additional copies of the nucleic acid molecules. Alternatively, the vector may integrate into the host cell genome and produce additional copies of the nucleic acid molecules when the host cell replicates.

The invention provides vectors for the maintenance (cloning vectors) or vectors for expression (expression vectors) of the nucleic acid molecules. The vectors can function in procaryotic or eukaryotic cells or in both (shuttle vectors).

Expression vectors contain cis-acting regulatory regions that are operably linked in the vector to the nucleic acid molecules such that transcription of the nucleic acid molecules is allowed in a host cell. The nucleic acid molecules can be introduced into the host cell with a separate nucleic acid molecule capable of affecting transcription. Thus, the second nucleic acid molecule may provide a trans-acting factor interacting with the cis-regulatory control region to allow transcription of the nucleic acid molecules from the vector. Alternatively, a trans-acting factor may be supplied by the host cell. Finally, a trans-acting factor can be produced from the vector itself. It is understood, however, that in some embodiments, transcription and/or translation of the nucleic acid molecules can occur in a cell-free system.

The regulatory sequence to which the nucleic acid molecules described herein can be operably linked include promoters for directing mRNA transcription. These include, but are not limited to, the left promoter from bacteriophage λ , the lac, TRP, and TAC promoters from E. coli, the early and late promoters from SV40, the CMV immediate early promoter, the adenovirus early and late promoters, and retrovirus long-terminal repeats.

In addition to control regions that promote transcription, expression vectors may also include regions that modulate transcription, such as repressor binding sites and enhancers.

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Examples include the SV40 enhancer, the cytomegalovirus immediate early enhancer, polyoma enhancer, adenovirus enhancers, and retrovirus LTR enhancers.

In addition to containing sites for transcription initiation and control, expression vectors can also contain sequences necessary for transcription termination and, in the transcribed region a ribosome binding site for translation. Other regulatory control elements for expression include initiation and termination codons as well as polyadenylation signals. The person of ordinary skill in the art would be aware of the numerous regulatory sequences that are useful in expression vectors. Such regulatory sequences are described, for example, in Sambrook et al., Molecular Cloning: A Laboratory Manual. 2nd. ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, (1989).

A variety of expression vectors can be used to express a nucleic acid molecule. Such vectors include chromosomal, episomal, and virus-derived vectors, for example vectors derived from bacterial plasmids, from bacteriophage, from yeast episomes, from yeast chromosomal elements, including yeast artificial chromosomes, from viruses such as baculoviruses, papovaviruses such as SV40, Vaccinia viruses, adenoviruses, poxviruses, pseudorabies viruses, and retroviruses. Vectors may also be derived from combinations of these sources such as those derived from plasmid and bacteriophage genetic elements, e.g. cosmids and phagemids. Appropriate cloning and expression vectors for prokaryotic and eukaryotic hosts are described in Sambrook et al., Molecular Cloning: A Laboratory Manual. 2nd. ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, (1989).

The regulatory sequence may provide constitutive expression in one or more host cells (i.e. tissue specific) or may provide for inducible expression in one or more cell types such as by temperature, nutrient additive, or exogenous factor such as a hormone or other ligand. A variety of vectors providing for constitutive and inducible expression in prokaryotic and eukaryotic hosts are well known to those of ordinary skill in the art.

The nucleic acid molecules can be inserted into the vector nucleic acid by well-known methodology. Generally, the DNA sequence that will ultimately be expressed is joined to an expression vector by cleaving the DNA sequence and the expression vector with one or more restriction enzymes and then ligating the fragments together. Procedures for restriction enzyme digestion and ligation are well known to those of ordinary skill in the art.

The vector containing the appropriate nucleic acid molecule can be introduced into an appropriate host cell for propagation or expression using well-known techniques. Bacterial cells include, but are not limited to, *E. coli*, *Streptomyces*, and *Salmonella typhimurium*.

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Eukaryotic cells include, but are not limited to, yeast, insect cells such as *Drosophila*, animal cells such as COS and CHO cells, and plant cells.

As described herein, it may be desirable to express the peptide as a fusion protein. Accordingly, the invention provides fusion vectors that allow for the production of the peptides. Fusion vectors can increase the expression of a recombinant protein, increase the solubility of the recombinant protein, and aid in the purification of the protein by acting for example as a ligand for affinity purification. A proteolytic cleavage site may be introduced at the junction of the fusion moiety so that the desired peptide can ultimately be separated from the fusion moiety. Proteolytic enzymes include, but are not limited to, factor Xa, thrombin, and enterotransporter. Typical fusion expression vectors include pGEX (Smith et al., Gene 67:31-40 (1988)), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein. Examples of suitable inducible non-fusion E. coli expression vectors include pTrc (Amann et al., Gene 69:301-315 (1988)) and pET 11d (Studier et al., Gene Expression Technology: Methods in Enzymology 185:60-89 (1990)).

Recombinant protein expression can be maximized in host bacteria by providing a genetic background wherein the host cell has an impaired capacity to proteolytically cleave the recombinant protein. (Gottesman, S., Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, California (1990) 119-128). Alternatively, the sequence of the nucleic acid molecule of interest can be altered to provide preferential codon usage for a specific host cell, for example E. coli. (Wada et al., Nucleic Acids Res. 20:2111-2118 (1992)).

The nucleic acid molecules can also be expressed by expression vectors that are operative in yeast. Examples of vectors for expression in yeast e.g., *S. cerevisiae* include pYepSec1 (Baldari, et al., EMBO J. 6:229-234 (1987)), pMFa (Kurjan et al., Cell 30:933-943(1982)), pJRY88 (Schultz et al., Gene 54:113-123 (1987)), and pYES2 (Invitrogen Corporation, San Diego, CA).

The nucleic acid molecules can also be expressed in insect cells using, for example, baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series (Smith *et al.*, *Mol. Cell Biol.* 3:2156-2165 (1983)) and the pVL series (Lucklow *et al.*, *Virology 170*:31-39 (1989)).

In certain embodiments of the invention, the nucleic acid molecules described herein are expressed in mammalian cells using mammalian expression vectors. Examples of mammalian

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expression vectors include pCDM8 (Seed, B. *Nature 329*:840(1987)) and pMT2PC (Kaufman et al., EMBO J. 6:187-195 (1987)).

The expression vectors listed herein are provided by way of example only of the well-known vectors available to those of ordinary skill in the art that would be useful to express the nucleic acid molecules. The person of ordinary skill in the art would be aware of other vectors suitable for maintenance propagation or expression of the nucleic acid molecules described herein. These are found for example in Sambrook, J., Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory*, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.

The invention also encompasses vectors in which the nucleic acid sequences described herein are cloned into the vector in reverse orientation, but operably linked to a regulatory sequence that permits transcription of antisense RNA. Thus, an antisense transcript can be produced to all, or to a portion, of the nucleic acid molecule sequences described herein, including both coding and non-coding regions. Expression of this antisense RNA is subject to each of the parameters described above in relation to expression of the sense RNA (regulatory sequences, constitutive or inducible expression, tissue-specific expression).

The invention also relates to recombinant host cells containing the vectors described herein. Host cells therefore include prokaryotic cells, lower eukaryotic cells such as yeast, other eukaryotic cells such as insect cells, and higher eukaryotic cells such as mammalian cells.

The recombinant host cells are prepared by introducing the vector constructs described herein into the cells by techniques readily available to the person of ordinary skill in the art. These include, but are not limited to, calcium phosphate transfection, DEAE-dextran-mediated transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, lipofection, and other techniques such as those found in Sambrook, et al. (Molecular Cloning: A Laboratory Manual. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

Host cells can contain more than one vector. Thus, different nucleotide sequences can be introduced on different vectors of the same cell. Similarly, the nucleic acid molecules can be introduced either alone or with other nucleic acid molecules that are not related to the nucleic acid molecules such as those providing trans-acting factors for expression vectors. When more than one vector is introduced into a cell, the vectors can be introduced independently, co-introduced or joined to the nucleic acid molecule vector.

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In the case of bacteriophage and viral vectors, these can be introduced into cells as packaged or encapsulated virus by standard procedures for infection and transduction. Viral vectors can be replication-competent or replication-defective. In the case in which viral replication is defective, replication will occur in host cells providing functions that complement the defects.

Vectors generally include selectable markers that enable the selection of the subpopulation of cells that contain the recombinant vector constructs. The marker can be contained in the same vector that contains the nucleic acid molecules described herein or may be on a separate vector. Markers include tetracycline or ampicillin-resistance genes for prokaryotic host cells and dihydrofolate reductase or neomycin resistance for eukaryotic host cells. However, any marker that provides selection for a phenotypic trait will be effective.

While the mature proteins can be produced in bacteria, yeast, mammalian cells, and other cells under the control of the appropriate regulatory sequences, cell- free transcription and translation systems can also be used to produce these proteins using RNA derived from the DNA constructs described herein.

Where secretion of the peptide is desired, which is difficult to achieve with multitransmembrane domain containing proteins such as transporters, appropriate secretion signals are incorporated into the vector. The signal sequence can be endogenous to the peptides or heterologous to these peptides.

Where the peptide is not secreted into the medium, which is typically the case with transporters, the protein can be isolated from the host cell by standard disruption procedures, including freeze thaw, sonication, mechanical disruption, use of lysing agents and the like. The peptide can then be recovered and purified by well-known purification methods including ammonium sulfate precipitation, acid extraction, anion or cationic exchange chromatography, phosphocellulose chromatography, hydrophobic-interaction chromatography, affinity chromatography, hydroxylapatite chromatography, lectin chromatography, or high performance liquid chromatography.

It is also understood that depending upon the host cell in recombinant production of the peptides described herein, the peptides can have various glycosylation patterns, depending upon the cell, or maybe non-glycosylated as when produced in bacteria. In addition, the peptides may include an initial modified methionine in some cases as a result of a host-mediated process.

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Uses of vectors and host cells

The recombinant host cells expressing the peptides described herein have a variety of uses. First, the cells are useful for producing a transporter protein or peptide that can be further purified to produce desired amounts of transporter protein or fragments. Thus, host cells containing expression vectors are useful for peptide production.

Host cells are also useful for conducting cell-based assays involving the transporter protein or transporter protein fragments, such as those described above as well as other formats known in the art. Thus, a recombinant host cell expressing a native transporter protein is useful for assaying compounds that stimulate or inhibit transporter protein function.

Host cells are also useful for identifying transporter protein mutants in which these functions are affected. If the mutants naturally occur and give rise to a pathology, host cells containing the mutations are useful to assay compounds that have a desired effect on the mutant transporter protein (for example, stimulating or inhibiting function) which may not be indicated by their effect on the native transporter protein.

Genetically engineered host cells can be further used to produce non-human transgenic animals. A transgenic animal is preferably a mammal, for example a rodent, such as a rat or mouse, in which one or more of the cells of the animal include a transgene. A transgene is exogenous DNA that is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal in one or more cell types or tissues of the transgenic animal. These animals are useful for studying the function of a transporter protein and identifying and evaluating modulators of transporter protein activity. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, and amphibians.

A transgenic animal can be produced by introducing nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. Any of the transporter protein nucleotide sequences can be introduced as a transgene into the genome of a non-human animal, such as a mouse.

Any of the regulatory or other sequences useful in expression vectors can form part of the transgenic sequence. This includes intronic sequences and polyadenylation signals, if not already included. A tissue-specific regulatory sequence(s) can be operably linked to the transgene to direct expression of the transporter protein to particular cells.

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Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, both by Leder *et al.*, U.S. Patent No. 4,873,191 by Wagner *et al.* and in Hogan, B., *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the transgene in its genome and/or expression of transgenic mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene can further be bred to other transgenic animals carrying other transgenes. A transgenic animal also includes animals in which the entire animal or tissues in the animal have been produced using the homologously recombinant host cells described herein.

In another embodiment, transgenic non-human animals can be produced which contain selected systems that allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, e.g., Lakso *et al. PNAS 89*:6232-6236 (1992). Another example of a recombinase system is the FLP recombinase system of *S. cerevisiae* (O'Gorman *et al. Science 251*:1351-1355 (1991). If a *cre/loxP* recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the *Cre* recombinase and a selected protein is required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut, I. et al. Nature 385:810-813 (1997) and PCT International Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G_0 phase. The quiescent cell can then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyst and then transferred to pseudopregnant female foster animal. The offspring born of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is isolated.

Transgenic animals containing recombinant cells that express the peptides described herein are useful to conduct the assays described herein in an *in vivo* context. Accordingly, the

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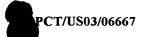




various physiological factors that are present *in vivo* and that could effect ligand binding, transporter protein activation, and signal transduction, may not be evident from *in vitro* cell-free or cell-based assays. Accordingly, it is useful to provide non-human transgenic animals to assay *in vivo* transporter protein function, including ligand interaction, the effect of specific mutant transporter proteins on transporter protein function and ligand interaction, and the effect of chimeric transporter proteins. It is also possible to assess the effect of null mutations, that is mutations that substantially or completely eliminate one or more transporter protein functions.

All publications and patents mentioned in the above specification are herein incorporated by reference. Various modifications and variations of the described method and system of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific preferred embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the above-described modes for carrying out the invention which are obvious to those skilled in the field of molecular biology or related fields are intended to be within the scope of the following claims.





Claims

That which is claimed is:

- 1. An isolated peptide consisting of an amino acid sequence selected from the group consisting of:
 - (a) an amino acid sequence shown in SEQ ID NO:2;
- (b) an amino acid sequence of an allelic variant of an amino acid sequence shown in SEQ ID NO:2, wherein said allelic variant is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3;
- (c) an amino acid sequence of an ortholog of an amino acid sequence shown in SEQ ID NO:2, wherein said ortholog is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3; and
- (d) a fragment of an amino acid sequence shown in SEQ ID NO:2, wherein said fragment comprises at least 10 contiguous amino acids.
- 2. An isolated peptide comprising an amino acid sequence selected from the group consisting of:
 - (a) an amino acid sequence shown in SEQ ID NO:2;
- (b) an amino acid sequence of an allelic variant of an amino acid sequence shown in SEQ ID NO:2, wherein said allelic variant is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3;
- (c) an amino acid sequence of an ortholog of an amino acid sequence shown in SEQ ID NO:2, wherein said ortholog is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3; and
- (d) a fragment of an amino acid sequence shown in SEQ ID NO:2, wherein said fragment comprises at least 10 contiguous amino acids.
 - 3. An isolated antibody that selectively binds to a peptide of claim 2.





- 4. An isolated nucleic acid molecule consisting of a nucleotide sequence selected from the group consisting of:
- (a) a nucleotide sequence that encodes an amino acid sequence shown in SEQ ID NO:2;
- (b) a nucleotide sequence that encodes of an allelic variant of an amino acid sequence shown in SEQ ID NO:2, wherein said nucleotide sequence hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3;
- (c) a nucleotide sequence that encodes an ortholog of an amino acid sequence shown in SEQ ID NO:2, wherein said nucleotide sequence hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3;
- (d) a nucleotide sequence that encodes a fragment of an amino acid sequence shown in SEQ ID NO:2, wherein said fragment comprises at least 10 contiguous amino acids; and
- (e) a nucleotide sequence that is the complement of a nucleotide sequence of (a)-(d).
- 5. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:
- (a) a nucleotide sequence that encodes an amino acid sequence shown in SEQ ID NO:2;
- (b) a nucleotide sequence that encodes of an allelic variant of an amino acid sequence shown in SEQ ID NO:2, wherein said nucleotide sequence hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3;
- (c) a nucleotide sequence that encodes an ortholog of an amino acid sequence shown in SEQ ID NO:2, wherein said nucleotide sequence hybridizes under stringent conditions to the opposite strand of a nucleic acid molecule shown in SEQ ID NOS:1 or 3;
- (d) a nucleotide sequence that encodes a fragment of an amino acid sequence shown in SEQ ID NO:2, wherein said fragment comprises at least 10 contiguous amino acids; and
- (e) a nucleotide sequence that is the complement of a nucleotide sequence of (a)-(d).
 - 6. A gene chip comprising a nucleic acid molecule of claim 5.



- 7. A transgenic non-human animal comprising a nucleic acid molecule of claim 5.
- 8. A nucleic acid vector comprising a nucleic acid molecule of claim 5.
- 9. A host cell containing the vector of claim 8.
- 10. A method for producing any of the peptides of claim 1 comprising introducing a nucleotide sequence encoding any of the amino acid sequences in (a)-(d) into a host cell, and culturing the host cell under conditions in which the peptides are expressed from the nucleotide sequence.
- 11. A method for producing any of the peptides of claim 2 comprising introducing a nucleotide sequence encoding any of the amino acid sequences in (a)-(d) into a host cell, and culturing the host cell under conditions in which the peptides are expressed from the nucleotide sequence.
- 12. A method for detecting the presence of any of the peptides of claim 2 in a sample, said method comprising contacting said sample with a detection agent that specifically allows detection of the presence of the peptide in the sample and then detecting the presence of the peptide.
- 13. A method for detecting the presence of a nucleic acid molecule of claim 5 in a sample, said method comprising contacting the sample with an oligonucleotide that hybridizes to said nucleic acid molecule under stringent conditions and determining whether the oligonucleotide binds to said nucleic acid molecule in the sample.
- 14. A method for identifying a modulator of a peptide of claim 2, said method comprising contacting said peptide with an agent and determining if said agent has modulated the function or activity of said peptide.
- 15. The method of claim 14, wherein said agent is administered to a host cell comprising an expression vector that expresses said peptide.





- 16. A method for identifying an agent that binds to any of the peptides of claim 2, said method comprising contacting the peptide with an agent and assaying the contacted mixture to determine whether a complex is formed with the agent bound to the peptide.
- 17. A pharmaceutical composition comprising an agent identified by the method of claim 16 and a pharmaceutically acceptable carrier therefor.
- 18. A method for treating a disease or condition mediated by a human transporter protein, said method comprising administering to a patient a pharmaceutically effective amount of an agent identified by the method of claim 16.
- 19. A method for identifying a modulator of the expression of a peptide of claim 2, said method comprising contacting a cell expressing said peptide with an agent, and determining if said agent has modulated the expression of said peptide.
- 20. An isolated human transporter peptide having an amino acid sequence that shares at least 70% homology with an amino acid sequence shown in SEQ ID NO:2.
- 21. A peptide according to claim 20 that shares at least 90 percent homology with an amino acid sequence shown in SEQ ID NO:2.
- 22. An isolated nucleic acid molecule encoding a human transporter peptide, said nucleic acid molecule sharing at least 80 percent homology with a nucleic acid molecule shown in SEQ ID NOS:1 or 3.
- 23. A nucleic acid molecule according to claim 22 that shares at least 90 percent homology with a nucleic acid molecule shown in SEQ ID NOS:1 or 3.





1 ATGGTGCTCT CCCAGGAGGA GCCGGACTCC GCGCGGGGCA CGAGCGAGGC
51 GCAGCOGCTC GGCCCCGGCGC CCACGGGGGGC CGCTCCGCCG CCCGGCCCGG
101 GACCCTOGGA CAGCCCCGAG GCGGCTGTCG AGAAGGTGGA GGTGGAGCTG
151 GCGGGCCGG CGACCGCGGA GCCCCCATGAG CCCCCCGAAC CCCCCGAGGG
151 GCGGGCCG CACCGCGA TCCTCCCCC CATCTCCTCC AACCCCTCCC
201 CGGCTGGGGC TGGCTGGTGA TGCTGGCGGC CATGTGGTGC AACGGGTCGG
251 TGTTCGGCAT CCAGAACGCT TGCGGGGTGC TCTTCGTGTC CATGCTGGAA
301 ACCTTOGGCT CCAAAGACGA TGACAAGATG GTCTTTAAGA CAGCAGCATG
351 GGTAGGTTCT CTCTCCATGG GGATGATTTT CTTTTGCTGC CCAATAGTCA
401 GCGTCTTCAC AGACCTATTT GGTTGTCGGA AAACAGCTGT CGTGGGTGCT
451 GCTGTTGGAT TTGTTGGGCT CATGTCCAGT TCTTTTGTAA GTTCCATCGA
501 GCCTCTGTAC CTTACCTATG GAATCATATT TGCCTGCGGC TGCTCCTTTG
551 CATACCAGCC TICATTGGTC ATTITGGGAC ACTATTICAA GAAGCGCCTT
601 GGACTGGTGA ATGGCATTGT CACTGCTGGC AGCAGTGTCT TCACAATCCT
651 GCTGCCTTTG CTCTTAAGGG TTCTGATTGA CAGCGTGGGC CTCTTTTACA
701. CATTGAGGGT GCTCTGCATC TTCATGTTTG TTCTCTTTCT GGCTGGCTTT
751 ACTTACCGAC CTCTTGCTAC CAGTACCAAA GATAAAGAGA GTGGAGGTAG
801 CGGATCCTCC CTCTTTTCCA GGAAAAAGTT CAGTCCTCCA AAAAAAATTT
851 TCAATTITIGC CATCTTCAAG GTGACAGCTT ATGCAGTGTG GGCAGTTGGA
901 ATACCACTTG CACITITITGG ATACTITIGTG CCTTATGTTC ACTTGATGAA
951 ACATGTAAAT GAAAGATTTC AAGATGAAAA AAATAAAGAG GTTGTTCTCA
1001 TGTGCATTGG CGTCACTTCA GGAGTTGGAC GACTGCTCTT TGGCCGGATT
1051 GCAGATTATG TGCCTGGTGT GAAGAAGGTT TATCTACAGG TACTCTCCTT
1101 TITICITICATT GGTCTGATGT CCATGATGAT TCCTCTGTGT AGCATCTTTG
1151 GGGCCCTCAT TGCTGTGTGC CTCATCATGG GTCTCTTCGA TGGATGCTTC
1201 ATTTCCATTA TGGCTCCCAT AGCCTTTGAG TTAGTTGGTG CCCAGGATGT
1251 CTCCCAAGCA ATTIGGATTTC TIGCTCGGATT CATGTCTATA CCCATGACTG
1301 TTGGCCCACC CATTGCAGGG TTACTTCGTG ACAAACTGGG CTCCTATGAT
1351 GTGGCATTCT ACCTCGCTGG AGTCCCTCCC CTTATTGGAG GTGCTGTGCT
1401 TIGTTITATC CCGTGGATCC ATAGTAAGAA GCAAAGAGAG ATCAGTAAAA
1451 CCACTGGAAA AGAAAAGATG GAGAAAATGT TGGAAAACCA GAACTCTCTG
1501 CTGTCAAGTT CATCTGGAAT GTTCAAGAAA GAATCTGACT CTATTATTTA
1551 A (SEQ ID NO: 1)
• •

FEATURES: Start Codon: 1 Stop Codon: 1549 2/65



HOMOLOGOUS PROTEINS: <u>TOP BLAST Hits:</u> TOP 10 BLAST Hits:

Sequences producing significant alignments:		E Value
CRA 62000057354769 /altid=gi 14090278 /def=dbj BAB55595.1 (ABO CRA 18000004921871 /altid=gi 5730045 /def=ref NP_006508.1 (NM CRA 18000004921870 /altid=gi 7513431 /def=pir 138495 X-linked CRA 18000005134802 /altid=gi 6677997 /def=ref NP_033223.1 (NM CRA 163000000492387 /altid=gi 8923981 /def=ref NP_061063.1 (NM CRA 224000009228679 /altid=gi 17389922 /def=gb AAH17968.1 AAH17 CRA 8900000201355 /altid=gi 7299667 /def=gb AAF54851.1 (AE003 CRA 22400007378350 /altid=gi 16768034 /def=gb AAL28236.1 (AYO CRA 18000005086356 /altid=gi 7449989 /def=pir JC5507 monocarbo CRA 18000005075554 /altid=gi 6226943 /def=sp Q90632 MOT3_CHICK	874 527 527 516 402 399 353 353 189 188	0.0 e-148 e-148 e-144 e-110 e-109 1e-95 1e-95 2e-46 4e-46

EST:

CRA Number	gi Number 	Score 1265 bits (638) 1170 bits (590) 1063 bits (536) 1049 bits (529) 1017 bits (513) 973 bits (491) 902 bits (455) 680 bits (343)	0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0
CRA 330000005235303	gi 6989741	551 bits (278)	1e-154
CRA 3000001439560	gi 1166011	547 bits (276)	1e-153
CRA 1000684940123	gi 6569405	486 bits (245)	1e-134
CRA 1000610791502	gi 5933739	486 bits (245)	1e-134
CRA 3000001441088	gi 1164256	462 bits (233)	1e-127
CRA 160000129872523	gi 13723263	410 bits (207)	1e-112
CRA 162000043366421	gi 10877364	234 bits (118)	8e-59
CRA 3000000874607	gi 2994619	218 bits (110)	5e-54
CRA 225000013398008	gi 18086759	208 bits (105)	4e-51

EXPRESSION INFORMATION FOR MODULATORY USE:

library source:		
gi Number	Organ	Tissue Type
gi 14568965	lung	small cell carcinoma
gi 6359768	(none)	liver
gi 13709362	(none)	(none)
gi 12788094	brain	neuroblastoma cells
gi 10813242	(none)	pooled germ cell tumors
gi 13460082	prostate	adenocarcinoma
gi 13720697	(none)	(none)
gi 11084182	ovary	fibrotheoma
gi 6989741	(none)	(none)
gi 1166011	placenta	(none)
gi 6569405	(none)	pooled germ cell tumors
gi 5933739	thymus, pooled	(none)
gi 5933739 gi 1164256	placenta	(none)
gi 13723263	(none)	(none)
gi 10877364	colon	(none)
gi 2994619	pooled	(none) _
gi 18086759	Pancreas	Islets of Langerhans

FIGURE 1B



PCT/US03/06667

```
1 MVLSQEEPDS ARGTSEAQPL GPAPTGAAPP PGPGPSDSPE AAVEKVEVEL
   51 AGPATAEPHE PPEPPEGGNG WLVMLAAMNC NGSVFGIQNA CGVLFVSMLE
  101 TFGSKDDDKM VFKTAAWVGS LSMGMIFFCC PIVSVFTDLF GCRKTAVVGA
  151 AVGFVGLMSS SFVSSIEPLY LTYGIIFACG CSFAYQPSLV ILGHYFKKRL
  201 GLVNGIVTAG SSVFTILLPL LLRVLIDSVG LFYTLRVLCI PMFVLFLAGF
251 TYRPLATSTK DKESGGSGSS LFSRKKFSPP KKIFNFAIFK VTAYAWWAVG
  301 IPLALFGYFV PYVHLMKHVN ERFODEKNKE VVLMCIGVTS GVGRLLFGRI
351 ADYVPGVKKV YLQVLSFFFI GLMSMMIPLC SIFGALIAVC LIMGLFDGCF
  401 ISIMAPIAFE LVGAQDVSQA IGFLLGRVSI PMTVGPPIAG LLRDKLGSYD
  451 VAFYLAGVPP LIGGAVLCFI PWIHSKKORE ISKTTGKEKM EKMLENONSL
  501 LSSSSGMFKK ESDSII (SEQ ID NO: 2)
FEATURES:
Functional domains and key regions:
PDOCO0001 PS00001 ASN_GLYCOSYLATION
N-glycosylation site
               81-84
                         NGSV
PDOCO0002 PS00002 GLYCOSAMINOGLYCAN
Glycosaminoglycan attachment site
                340-343 SGVG
PDOC00004 PS00004 CAMP_PHOSPHO_SITE
cAMP- and cGMP-dependent protein kinase phosphorylation site
Number of matches: 2
               275-278 KKFS
       1
        2
               509-512 KKES
PDOCO0005 PS00005 PKC_PHOSPHO_SITE
Protein kinase C phosphorylation site
Number of matches: 7
               10-12
                         SAR
                234-236 TLR
               251-253 TYR
                258-260 STK
               273-275 SRK
       5
                475-477 SKK
               485-487 TGK
PDOCO0006 PS00006 CK2_PHOSPHO_SITE
Casein kinase II phosphorylation site
Number of matches: 6
                4-7
                         SOFE
               97-100
                        SMLE
       3
               104-107 SKDD
       4
               164-167 SSIE
       5
               258-261 STKD
       6
               485-488 TCKE
PDOCO0008 PS00008 MYRISTYL
N-myristoylation site
Number of matches: 15
               13-18
                        GTSEAQ
               82-87
                        GSVFGI
               141-146 GCRKTA
               149-154 GAAVGF
               156-161 GLMSSS
       6
7
               174-179 GIIFAC
                180-185 GCSFAY
               201-206 GLVNGI
       8
       9
               230-235 GLFYTL
       10
               265-270 GGSGSS
               300-305 GIPLAL
337-342 GVTSGV
       11
       12
       13
               384-389 GALIAV
```

394-399 GLFDGC

464-469 GAVLCF

14

FIGURE 2A



PDOCO0013 PS00013 PRCXAR_LIPOPROTEIN
Prokaryotic membrane lipoprotein lipid attachment site
169-179 LYLTYGIIFAC

PDOC00029 PS00029 LEUCINE_ZIPPER
Leucine zipper pattern
365-386 LSFFFIGLMSMMIPLCSIFGAL

PDOC00240 PS00267 TACHYKININ Tachykinin family signature Number of matches: 2 1 154-158 FVGLM

1 154-158 FVGLM 2 369-373 FIGLM

Membrane spanning structure and domains: Helix Begin End Score Certainity 87 1.683 Certain 67 2.220 Certain 1.923 Certain 2 117 137 3 146 166 1.494 Certain 4 169 189 5 202 222 1.761 Certain 6 7 232 252 1.893 Certain 291 311 1.874 Certain 0.801 Putative 8 9 330 350 364 384 2.458 Certain 10 387 407 1.707 Certain 1.966 Certain 11 419 439 473 1.826 Certain 453

Score = 874 bits (2233), Expect = 0.0 Identities = 435/517 (84%), Positives = 463/517 (89%), Gaps = 1/517 (0%) Frame = +1

Query: 232 M/LSQEEPDSA-RGTSEAQPLGPAPTGAAPPPGPGPSDSPEAAVEKVEVELAGPATAEPH 408 M/ S EEP +A R T+EAQP GPAP+ AP P PGPSD + +VEKVEVEL +

Sbjct: 1 MYPSLEEPAAAERETNEAQPPGPAPSDDAPLPVPGPSDVSDGSVEKVEVELT--RSTGNQ 58

Query: 409 EPPEPPEGGWGWLVMLAAMWCNGSVFGIQNACGVLFVSMLETFGSKDDDKMVFKTAAWWG 588 EPPEPPEGGWGWLVMLAAMWCNGSVFGIQNA GVLFVSMLETFG+KDDD M FK AAWWG

Sbjct: 59 EPPEPPEGGNGNLVNLAAMWCNGSVFGIQNAYGVLFVSMLETFGAKDDDNMAFK-AAWWG 117

Query: 589 SLSMGMIFFCCPIVSVFTDLFGCRKTAVVGAAVGFVGLMSSSFVSSIEPLYLTYGIIFAC 768
SLSMGMIFFCCPIVSVFTD+FGCR+TAV+GAAVGFVGLMSSSFVSSIEPLY TYG++FAC

Sbjct: 118 SLSMGMIFFCCPIVSVFTDMFGCRRTAVLGAAVGFVGLMSSSFVSSIEPLYFTYGWFAC 177

Query: 769 GCSFAYQPSLVILGHYFKKRLGLVNGIVTAGSSVFTILLPLLLRVLIDSVGLFYTLRVLC 948
GCSFAYQPSLVILGHYFKKRLGLVNGIVTAGSSVFTILLPLLL L +VGL YTLR+LC

Sbjct: 178 GCSFAYQPSLVILGHYFKKRLGLVNGIVTAGSSVFTILLPLLLGNLTSTVGLCYTLRILC 237

Query: 949 IFMFVLFLAGFTYRPLATSTKDKESGGSGSSLFSRKKFSPPKKIFNFAIFKVTAYAVWAV 1128 IFMFVLFLAGFTYRPL S+K+KES S SS FSR+K SPPKKIFNFA+FK TAYAVWA

Sbjct: 238 IFMFVLFLAGFTYRPLVPSSKEKESEDSRSSFFSRRKLSPPKKIFNFALFKETAYAVWAA 297

Query: 1129 GIPLALFGYFVPYVHLMKHNNERFQDEKNKEVVLMCIGVTSGVGRLLFGRIADYVPGVKK 1308 GIPLALFGYFVPYVHLM HV ERF+D NKEV+ MCIGVTSGVGRLLFGRIADY+PGVKK

Sbjct: 298 GIPLALFGYFYPYHLMNHKERFKOMNKEVLFMCIGVTSGVGRLLFGRIADYLPGKK 357

Query: 1309 VYLQVLSFFFIGLMSMMIPLCSIFGALIAVCLIMGLFDGCFISIMAPIAFELVGAQDVSQ 1488
VYLQVLSFFFIGL SMMIPLCS+FGALIA+CLIMGLFDGCFISIMAPIAFELVG QD SQ



Sbjct: 358 VYLQVLSFFFIGLTSMMIPLCSVFGALIALCLIMGLFDGCFISIMAPIAFELVGPQDASQ 417

Query: 1489 AIGFLLGFMSIPMTVGPPIAGLLRDKLGSYDVAFYLAGVPPLIGGAVLCFIPWIHSKKQR 1668 AIGFLLGFMSIPMTVGPP+AGLL DKLGSYD+AFYLAG+PP IGGAVLC IPWIHSKKQR

Sbjct: 418 AIGFLLGRYSIPMTVGPPVAGLLHDKLGSYDLAFYLAGIPPFIGGAVLCLIPWIHSKKOR 477

Query: 1669 EISKTTGKEKMEKMLENQNSLLSSSSGMFKKESDSII 1779

EISK TG EKMEKML NQ+SLLSSSSG+FKKESDSII

Sbjct: 478 EISKNTGGEKMEKMLANQSSLLSSSSGIFKKESDSII 514 (SEQ ID NO: 4)

Hmmer search results (Pfam):

Mode1	Description	Score	<u>E-value N</u>
PF00664	ABC transporter transmembrane region.	4.2	7.1
PF01027	Uncharacterized protein family	3.4	7.6 1
PF00083	Sugar (and other) transporter	2.0	7.4 1

Parsed for domains:

Model	Domain	seq-f	seq-t	 hmm-f	hmm-t		score	E-value
PF00083	1/1	11	50	 184	223		2.0	7.4
PF01027	1/1	121	177	 1	59	[.	3.4	7.6
PF00664	1/1	165	232	 1	76	Ĩ.	4.2	7.1





				-,	
1	AATGGGTATT	TTGTAGACTG	TCCTTGATTG	GGATTTGTCT	AATGTTTTC
	TGATGGTTAG				
101	AGTACCATTT	TCATCACATC	ATATCGGGGA	TACATTATCA	TCTAGTTGAG
151	GTACTGTGTG	CCATTTTTG	CACCCTAAAG	TTATTTCTTC	CCCCCACTCC
201	CCCTTTCCAT	CCTATACTCT	TTGGAAGAAA	GTTACTACGC	ATACCCACAC
251	TTAAAGAGTA	AACCATTGTA	CTTCACCTCC	ATGAGGGAGG	GAGTATGTTC
301	ATAAAGTATT	TACATTTCCT	GCAGGAGAGA	TTTGTCTATT	CTCTCCTCAT
351	TATTTATTTA	ATCATTTACT	TACATCAGTA	CTGACTCGTG	GATAATTCTT
401	ACATATGTGT	गाजागजाज	GCATGCAAAT	ATATAATCGA	TGIGCTTTCT
451	TTGCCCAATA	ATATGTTGTG	GACAACTTTC	AAAGTCAATA	AATACAGATG
501	ACCTTCAGAA	CTTTTAGAGG	TTTTAAAGTA	AGTATCTAAT	CAGTCTTCTA
551	CCAATGTACA	TTATACTTCC	AAATTTTCCT	TATTICCAAC	AATACTGGGG
601	TATCATCTTC	ATACATACAT	TTTTGTGCAC	TTATGTGCCT	ATTCCTTTGT
651	TTACTATTTT	ACCCTCATTT	CTAAGGCAGA	TIACACTIGA	GCIAIGITCC
\OT	CCATTCCACA	ACCAAGCACG	GCTTGCTTTC	CHAGITIAL	CCTATCTATC
/2T	CTACCTGGAA	TECCECAAAC	CIGICIIGAC	CTACACCCTC	TTCTACACTC
POT	AATCAGGGCT TTTGGAGAGA	ATTTAACCCA	CTATCTCATC	TOTOTOTOTO	CTACATCTAT
	TATAACACAT				
901	ACCAGTTTAT	CAACTIGAGGC	CACCCACAAA	CCAGATCAAT	CCACTCATC
1001	TGTGTACTCT	ATTACACTEG	TICCCCACATC	AAGTAACTAG	CATATTTIGA
1051	CTTTGATTGA	ACTGAAGAAT	ACGAATAACA	GAAATTAAGA	AGCATCCTCA
1101	ATATTGCATA	CAGGITACT	CHICHICI	TTTACATAGG	ATGGCACTCC
1151	ATGCTTCAGG	GAGACAGAGG	AGTTGAATAC	AGGITTIAGT	TITIGITIAA
1201	AGTGAAAACG	ACTICIGATI	AGTTGAAAAG	TAATGCTTTC	TAGCTGTCTG
1251	TTAAAAATGT	TIGITGGITG	AAGACTTCGG	AATTGCAGTC	CAGTGAGGAC
1301	TGAAAATAAG	CATCTTTGGT	GTGCCAAATA	TTCATAAGGA	AATTGTATAC
1351	GAATGCAAGA	GAATGGAACT	GAAGTAATAA	AATAAGGGCT	CTGATCCTTC
1401	AGATGACTTA	TTTAAGAAGC	CAGGTGGCAT	AACGAATCTT	ACATATTATA
1451	ATTAGTACTG	AGAGGTGAAT	GCCAAAACAT	AAAACAAACA	CAATCGAGAC
1501	AATGTTAGTG	TGACTGTGAC	GCTGTGTCGG	TGAGTTGAGG	CTAACGATCC
1551	AGTGTGGCTC	TCCTGAAGGC	CCACCGCGCC	CGCACCTAGG	AGACGCGCCC
1601	CTTCTGCTCA	TGCTTTGAGG	CGGGGTGACC	CACACATCTG	TGCCCCTCTC
	TGAGCAGGAG				
1701	CGGGCACCTG	GGGCCGCG	CCGCGGGGCG	201222020	GCTCTCCGAG
1751	GCCCAATCAT	CTGGAGGCTG	TGGGGGCACG	TCCCGCTCCC	GGCCACGCCC
T80T	CCAGCCGGCG	CCCCCCCCCC	IGCITTAAG	AACCGGGGGC	TOGCAGIGGG
182T	CTCAGTCGGG	GGIGGGGGC	IGIGACCIAG	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	CCCCCCCCCC
1901	CCTGCGCGCT	CCCACCCCCC	CIGICCICGC	CCCCCTCCCC	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC
7001	TCGGCCTCGT	TACCCCCCCA	CCACCCCCC	ACCTICATION	CCACCCCCCT
2001	GGTAACTCGC	CITCOTTOCC	CTICTCCCCC	CCTGAGGG	CCCCCCCCC
2101	GCCATGGTGC	TCTCCAGGA	GEAGCCGGAC	TCCCCCCCC	GCACGAGCGA
2151	GGCGCAGCCG	CTCGCCCCG	CCCCACGG	GCCGCTCCG	CCCCCCCCCC
2201	CGGGACCCTC	GGACAGCCCC	GAGGCGGCTG	TCGAGAAGGT	GGAGGTGGAG
2251	CTGGCGGGGC	CGGCGACCGC	GGAGCCCCAT	GAGCCCCCCG	AACCCCCCGA
2301	GGGCGGCTGG	GGCTGGCTGG	TGATGCTGGC	GGCCATGTGG	TGCAACGGGT
2351	CGGTGTTCGG	CATCCAGAAC	GCTTGCGGGG	TECTCTTCGT	GTCCATGCTG
2401	GAAACCTTCG	GCTCCAAAGA	CGATGACAAG	ATGGTCTTTA	AGACAGGTGA
2451	GCCGCGGCGC	CCGCCGAGGC	CAGCCTGGGC	GACCCGCGTG	GGGCCCCCGA
2501	GCGCATCCCG	CGTGTGGGCT	जजटाख्टरा	CCGAGTGTGC	ATGTCGGTGG
2551	GTCCCTGTGC	CAGAGGGTGC	GAGCAGGGGG	GICTTICGAG	TTGCAGACAG
2601	AGCCTGCCGC	TTCTGGGGCC	TCGGGGTGCC	CGTCTTTATA	TGGAATCCAG
2651	CTGCAGAGCT	GIGIGITICC	AAGCAGGTCG	CAGAACTTAC	TIGCCGAGAT
2/01	CGTCCTCCTT	TCCCCTCAGC	AGAGCAGACG	CIAACAGICC	ACAGGAGCCC
5/2T	TICCITITAT	TGTTTGAAAA	CANACAGAAC	CCCAGAACCI	CACTTATO
700T	TCATCGCCCT AGTTCTTCAC	GICATTIIG	CCCCCCACA	CCCCTTTCC	TATIETTECCE
2001 1001	GGGCGGGGGG	CIGCICCI	ACCAATICAAA	CACATTTCTA	CCAACCTCAC
20E1	TGGAGTTCCA	AVCCCCCCCC	TICCAACACTIC	ACCEPTACE	CCCTTCCCT
3001 733T	CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCC	TITITICAL	TOTOTOTO	ΔΤΩΤΑΓΑΛΑΛ	CACCCCACC
3021	AGCCGGATTA	CCCACTACCA	TCACCAACCT	CAPCCCLLUC	HCHICCIC
3101	TICCIGITG	GITTICAC	ATTITITIT	AACCATATAG	TAAATTAGAT
3151	ACAAAAGGTG	CAGATTCAGC	GTTTCTCCC	TGTAGAGCAT	TATTATGACT
3201	TITTEGETEG	TTAGGCAAAA	AACAAATCTA	AGACCTTCTG	CATGACACTT
3251	TAACATAAAT	TCTTTCACTT	TATCCTGCAA	GGTGAGCGCG	GTCAACCCCA
3301	TTTGGGTGAG	AAAACTGTAG	CTCAGTGAAA	GIGICITIGGI	GGGTAGTAGA
3351	ATGGCAATAA	AACACATATC	AACTGACTTC	AAGGGCTAAG	TGATTTCCAT



7/65



3401 TACTAAATCA ACCTCCCTCC CCATCATTTG GGGTAACTTT ATATGATTAA 3451 TAGTCTTTTT TTTTAACCTT GATTTTCTAT TATTTTTAGA GTGAATATTT 3501 CTTAGGTCTT TAGTATGCAT ATGAGGAATG GGCAAGACTG TAATAAATTC 3551 TGAGACAAAG GTAATGCTGG GTTATGCTGA GAGTTTTAAA ACCTGACATA 3601 AATACTATTA AACTATTTGT ATCATTCTGC AACTTACTTT TCTTCCATTC 3651 CGCATCATGT TTGTGACTTA TCCACATAAT ACCTCAGTGT GAACTGATAA 3701 CTCAAATTCT TTCCATTTTA ACTTAGGTGG TTTGCATTGT TTGACTATAT 3751 TATACTCTAT GCATTCTCCC TCTGATGGGC ATTTAGATTG CTTCCAAACT 3801 CATTCTAAAC AATGCTGCAA TGAATATTCT TGTACACTCT CGTTATGCAT 3851 GTGAATACGG TACCATTTTA ACCTGGAATT TCTGTTCTTT AAATAGCTAT 3901 TGAAACTGCT GTGGTATGCG GGTCAATGGG CTAGGTACAA AAAGTGTTAA 3951 AAATGTAGTA ACATATOCTT ACCATTTAAG GGAAGTAATC ATTGTAAAGT 4001 TTAGCAGGGG AGATATGCAT ATATAATAGC AAACAAAAAT AGTTTGTTGT 4051 CTTTTCTATA TGAGTATTGG GTGTCAGAGA GAAAAGCCCC AAAAGAAGGC 4101 AGAATTGACA GAGTTAACAT TTAAAGACTA GTTCCAACAT TTACCATATT 4151 CCTGCCTGGG ATTACAGATT TTTTAATGCA GTCAAGATAA CAGCAGTCTT 4201 TIGITTATCA TIGITTITGC AAATTCAGTT AAGTAGATCC TTIGGTGTCT 4301 AGAGAGAGAG AGCAATTGCC AGAGAGACCA TAGCTTTGCC AGGGATGAGA
4351 ATTTTGCAGT GTCAAAGTCT CTACCTACTA CTTGTCCCCA AAGTTCTAAT 4401 TGGCTACACA ATATCCCAAT ACTGGGTAGC TGAGAGTGAG GGAAGGAACC 4451 TGGTTTTTCT TTTGCACTCT GTGGAACTTT GTGTTTTCCA TTTTGATGAA 4501 TATCTTTTTT CTTTTTACTC AGTTCAGTCT TTGACAACTT TTTCAGTCAT 4551 GTTTGTGTAT GTGTGGGTAT ATATCATATA AACAGTTGCA CAGGTGTGCT 4601 AGTTAAATGT GTGAAGATCT TTGTGTTTCT CTGCCTGACT GCTGTATATC 4651 TATTTATGGT TGTGCCATTG CACAAGGGTG CCCAACTCAG GGGTAAGTGG 4701 GGACTGAAAA CCAGCCTGGG CTCTGGGTGC CCTTTGTCTG ATTCCTACAG 4751 AAGGGCCCTA TGCACTTGTA ATGGCCCTGT ATAACACAGC ATCTAGATTG 4801 AACAATGGCC ATTACTTGGG TGCTAGGTAA TACATATATG ACTGATAGAT 4851 GTTAAGGGCT GAGGAAGAAA ACAGATTTAA ACTTAGTGCT GAAAAAATGG 4901 TTACAAGATA GTCTTTAAGC CAGTTATTGT TGAGATCTCT CTCTCTTCCC 4951 CTGTCCCCTA CCCCTTTCTC TTTCCTTCAG TGCACACACA CACACACAAA 5001 GGTGTTTCAT GAAGTCCCTC ATCTACCACA GTCACTGTTA TTTGAGAATA 5051 TCTGCTTTGA AGTTTGATTG GTCACACTTT TTCACTTTGA TATTCGAATG 5101 CTGAGTCGTC TGTGATCAAG CATATGCAAG CTTCAAATAC ATGCCAAAAA 5151 ATATCTGGAA TTTGTTTAAG CCTTTTATTT TTCAAAGTTT TGGTCTATTT 5201 TCTATTACCG TACTCATGAT GGATAATCCT GGTGTTAGAG TACAGCTAGT 5251 TCTGTCTCCT TGTTTCCATT ACTTCTTTAT AGCAAGTGAC TAGCCTAAGG 5301 ATATACAGGG AGGTGGTGGT GGAATGGAAT CTAGGTCTCC AAATGATGGT 5351 GOGCATTTCT TGAGTACTTT CCTGTGGCTA AGCACTTTAG ATGCGTTCCT 5401 ATTTAAACCT TACCACGATT CTCTGATAGA CTTTGTTAAT ATCTTTCTTT 5451 TCAGATATGG GAACTCAGGC TTACAGAGTT TAAGTAAGAA GTGGAGCCAG 5501 AATTCAACCC CAGGCTTATC TGACTCTAAG AGCTGGGATT TTTATTTTAA 5551 TTATTTATTT ATTTAAAATA TGGAATGCTT CATGAATTTG CATGTCATCC 5601 ttigttcaggg gtcacgctaa tcttctctgt gtcattccaa ttttagtaga 5651 TIGTIGTICA AAGTGCTGCT GAAGCAAGCA CCAGGAGCTG GGTTTTAATC 5701 ATTCATCATA TIGCATIGAC TAGATAACAT TCTGCAAATA CGATGTTTTT 5751 tatigitigitig attaatittaa giigitagiiga titggitigagi gctictaccat 5801 GCATTCTGGG ATTAGAAAGA AGGGTCCCTG TTTCTTGGTC CTACTTTGTG 5851 GTGAATAAAC AATTGCAAAT TATTAATGTC TCAAACTATA TTTCTGAAGT 5901 GTAGAGAGAC TTCCATAGAA GAACAAGATA CTTCCATATG CCGTTCAAGC 5951 AAAAGTCTGG GGTTTCCTTT GAAGAACTTT TAGATTGATC CACAGCAGGA 6001 CAATGTTTCT AGGCAGAACT GAGGAGGAGC CTTTCTTAGG CTCACTTCTC 6051 TTCAGGGCTC TGTTAACTCT TCCCACGCAA TGGATAATCT ACCCAAAATT 6101 TCTCAGGAAA GGGCCTGAAG AAGTTCATTC ACACTAAGGT GTAAGTGAGT 6151 TTACACATCT TACTGTTAAT TCTCTTTATA CAAATGTTTA CCAAGTTATC 6201 TAACACISCTT TIGTTTTIGGIC TICTIGTICCTIGG GGACTIGGAGA TAATIGACTIGA 6251 GAGAGAAAAT GTCAGCTIGTT TICAAAGTAGIC TTAGGATICTIG TTIGTIGGGATA 6301 CAAATTAATA ACAGACCAGA AGTAATAGAA TATTTCCCTG AAGGATTTTC 6351 AATATAACAG GACTCAGTTT TACTATAAAA GGCTGAAATT CTAAGGTCAT 6401 TTCAACAGGT GGTGGGGTTG GGGGTGGGGA AGGCATTTGA CGCCTCTTTC 6451 TCTATGGTTA TAAATCTCAC TTGGTGAAAT TAAGACTTTG GAAAGGGGAA 6501 GTAAGCCAAC TCCAAGTTGG GCAGTAGAAC CAATGAAAAA TGCTGACGGC 6551 ATCACAGTCC CATTATGGTG CCCAGCTGCC AATGACATGG CACTCAGAGG 6601 AGTGTCTCAC ACATACTGCT CTGTCTGAGG GAGCAAGCTA AGCTTGAGTT 6651 GTCTCTTTT TTGTTGTTTT TTTTTTTTTTTTTTTGA GACAGATTCT 6701 CACTICTIGTOG CCCAGGCTGG AGTGCAGTGG CACCATICTCG GCTCACTGCA 6751 ACCACTGOCT CCCGGATGCA AGCAATTCTG CCTCAGCCTT CCGAGTAGCT



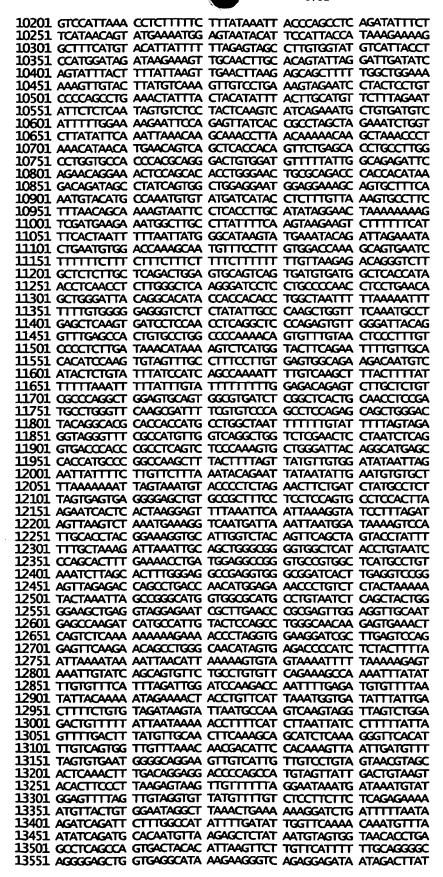




6801 GGACTACCTG CGCTTGCCAC CACACCTGGC TAATTTTTGT ATTTTTAGTA 6851 GAGACAGGGT TTCACCATAT TGGCCAGGCT GGTCTCAAAC TCCTGACCTC
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6951 CACCGCGCCT GGCCAAGTTG TCTCTTTTTA GTTGAATTTT TACCTGTTCA 7001 CATGTGTATT CTTCTTGCCT AGGTAGAGAG GAATCAGACA CTCTGGGGAA 7051 GAATACAAAG AAATACAATT AAGTGGAACA TTGTTTTTCT TTAGAAAGTG 7101 CAATTTTGGG CTGGGCGCAG TGGCTCATGC CTGTAATCCC AGCCCTTTGG
7151 GAGGCCAAGG CAGGTGGATC ACCTGAGGTC AGGAGTTTGA GACCAGCCTG 7201 GCCAAGATGG TGAAACCCCG TTTCTACTAA AAATACAAAA AATTAGCTGG 7251 GCATGGTGGC GGATGCGTGT AATCCCAGCT ATTCGGGAGG CTGAGGCAGG 7301 AGAATTIGCTT GAACCTIGGGA GGCAGAGGTT GTAGTIGAGCC AAGATIGGCGC 7351 CACTGTACTC CAGCATGGGC AACAAGAGTG AAACTCCGTC TCAAAAAAA 7401 AAAAAAGAAA AGAAAAAAAG AAAAAAGAAA GAGCAACTTT GTTTTAACTC 7451 TGCTAGATAC TGGAAAACCC ATGGAACTAA TGAAGAGCCT AGGGCTTTTT 7501 ATTTGTTTTG AGATTGTGCC ATTTCACTCC AGCCTGGGCA ACAAGAGAGA 7551 AACTTIGTCT CACACACAAA AAAAGTGTAA ATCAAAACAT TAAAAATTAA 7601 GTAGTTTGGA AGTAGATTAT CAAAAAGGTC CTGAAAGGGA GGTTCTTTGG 7651 CTATAATCTT TAACGCAACT CTACACTCCC TGTATGGAGA CAGATTTCTT 7701 TTTAGATGGT TACAGTCACA AAGTAGGGTT TTCAGTAGCA TTTAGGGATG 7751 AATGAATCTT GCAGCACCTC TCCATGTATC TTGCTAGCCC CTCTGAAACT 7801 TCAGGTCAGT TAGTGCTTCC TCAGAAATTG TTCCCCCCAC ACCAAGTTTT 7851 CACATTTACA GTTATACTGA TATCCACATT GTACTGTTGT ATGTGACACC 7901 TAGATTATAG GAAATTTTGG CTATAGTTCA GAAATTAACT GCTATGTTTT 7951 GCCTTTACGC TAAAGAGATT TTGTTTTGTT TAGTAGGAAA AGCGGCCTGC 8001 ATAACTAGCC ATTTCTGTAT CTTAGAAAAA TTTTTAGTAA CAGTCCTTTG 8051 TTGAGCTAGT TACAGTGAAC AAATAATCTG GTTCATGGTC CTATACATCT 8101 TTCACTATAA GAAAAATACC TGATTGTTAT TTACACTGGA AGAGAGGTAG 8151 AAAAGCTAAG AGAACTCACT TATGGCAATA AACCAATCTA AACTACCTGC 8201 TAAAATAAGT GAGAAGATTA TAAAAATGGT TCTAGGATTT TGGAATAATA 8251 GTGAGTATGG TATGGGCGTT TCATACTTCA TTTCCAGAAT GTTTCTGGAT 8301 TAAGTGCGAG ACTGAATAGC ATATATAGTG AATTCTAATT AAATACAACA 8351 ATGTGAGATT CCTGTGGTGT TTTTTCATGG AATTAAAAAT TAATAATTTC 8401 AATAAAATTA ACTGCTGAAA GAACCCAATT AGCCAAAATG AAAAGCATAA 8451 CACATTITIT CAGGAGCGAT TITGAGGTGT CTTTTAGAAT AAATTGTACT
8501 CTGCTTTTGA TGTGATTTGC TACATCTTTT TGTTGCAGTT CCTTGAGGCT
8551 CAGCCCCTGG CCATATACTT GCTTCACTTT TCCTGCTTTC TTCCATCCAC
8601 TGTCTTGGGG CTGTTATTTC CAAATCTCAT CACTGTGTTC AAGACTTATT 8651 TACTATTICT GGACAGTICC ATTIGGGTAC ACAGGTACAT CATACTAAAC 8701 TAACATGAAC TCATTITICA GCTACACCAT ACAACCTICC CTTACTACCA 8751 AAAATGACAG CCCATTIGIC GGCATICITC TGAATCCATA TICCTCCTIC 8801 TTAATTCTCT GTGCATGATA CCTCTGGTTG TTTAAGTCAG AAACCTGGAA 9251 CAAAGTGTTG GGACTACAGG CGGGACCTAC TGTGCCTGGC CACCTTCATT 9301 ACTATTGGCA ACAATTAGTC ATAACCCCTT AACAGGATTG CTTGTCCTCA 9351 GTTGTACATC TGAGTGATTT TTCTAAAAGA TTGGACCATA TGATTTTTCT 9401 GTTTAAATGC CCAGTGACAC TCATTACTTT TAGGAAAATG TCAAACTCCC 9451 TACTCCGAAG GCCTGCAAGC TCTGGCCCTT GCCTGGCCCT CTAGCCTTGC 9501 CCCTGCTTCT CTCCCTTACT GGTCTTTGTG TTCTAGCCAA CCTGTAGGTG 9551 TTACACTOGIC CCAAATTTIGT CTTGCTGCTT TTTGCCTCTG TACCTTTGTG
9601 TGTGCCACTC CTGTCTTCAG TGCGATGGTT GGTCCTTGTG AGATTCTGAT
9651 GAAATGGTTG GCCATTTTAT TCTTATGTCA CAATCCTGGG ACACAAACAG 9701 TGATTITATG CAATTGTTAT GTATTTGATG CACTTGGAAT ATTGGGGGTA 9751 GCTACATTTT GGAGTTTTGA GAACGAATTC AAATAAGTTA CAAATTATGT 9801 TTAAAGTGGT AGACAGAGAA CCTGATTTCA ACCTATTCTA ATAAAGCATT 9851 CCGTGAAAGC CATTTTAAAG ATGATCCATA TTTGTTAAAG TGGTAATTTT 9901 TATATTICTOT GATATIGGTTT GGCTGTGTTC CCACCCAAAT CTCATCTTGA 9951 ATTIGTAGCTC CCATAATCCA CACTTIGTCAT GGGAGGGAGG TAATTACCTG 10001 GTGGGAGGTA ATTGAATCAT GGGGGCAGGT TTTCCTGTGC TGTTCTTGTG
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13651	ΤΔΔΑΤΔΑΤΤΤ	GTATGTATGT	ATTTATTTAT	TTTTGAGACT	GGTCCTGCT
13701	CTECTECCCA	CCTCAACCG	TAGGGGTATG	AACACAGCTC	ACTGCAGCCT
12751	TEACCTEGGG	TCAAGGGATT	TTCTTGCCTC	ACCUTCCCGA	GTAGCTGGGA
13901	CCACACCCAT	CTCCCACTAC	ACCTGGCTAA	TTTTAAAGT	TITITIGIAG
130E1	ACATOCCCTC	TCACCACCTT	GCCCAGGTTG	CICTICAACT	CCTCCCCTCA
12001	AGAIGGGGIC	COCCOCC	CTCCCACACT	CTTCCCATTA	TACATICTCAC
1330T	AGCAATCCTC	CIGCCIIGG	CTCCCAGAGT	GIIGGGAIIA	CCEATCHCC
			ATAATTTCTA		
			AGGCTATTTT		
14051	CAGAATCTCA	GAGGGTTTTT	ACCTGCATTA	AAAATGATTA	AGGCTGGGCA
14101	GAATGGCTCA	TGCCTGTAAT	CCCATCACTT	TGGGAGGCTG	AGGCAGATGA
14151	ATTGCTTGAG	CCCAGAAGTT	CTAGAGCAGC	CTGGGCAACA	TGGTGAAACC
14201	CCATCTCTAC	GAAAAATGCA	AAAATTAGCT	GGACGTGGTG	GCAGGCACCT
14251	GTAGTCCCAG	CTACTCAAAA	GGCTGAGGTG	GGAGGATCAC	CTAGCTCTAG
14301	AGGTCAAGGG	TGCAATGAGC	CAAGATTGCT	CCACTGCCCG	CCAGCCTGGG
			TCAAAAAAA		
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14501	ATTACTICTAT	TTATEGETCA	CCTGGAAGAT	TCTTTATAAA	ACATGAGAGT
14551	TTATTACTTC	TTTCAATACA	CGGGTGTCTG	TAAATGATGC	TCAATAGATC
14601	TEAACCETCA	ACTITICICAA	GAAATGTTGT	GAAATTATCT	ATGGATGTCT
			AAATTGTAAT		
14701	TCAATTTCTA	ATTATTTCCC	GATTIGGATT	TOCTOTATO	ACAGITICICI
14701	TUTTION	COCCACTCE	CGCTTTGTCA	CCACCCTCCA	CICCACITICI
14/01	COCATO	CTCACTCCAA	TCTCTGCCTC	COCTCTACAA	CCCATTCTCC
14001	GUSAICIUG	CICACIGCAA	CTAGGATTAC	ACCCATICAC	CTCCATCCCC
14001	IGCTTAGCT	TOCTOAGTAG	CTAGGATTAC	CCTTTCACCA	TOTALOGGE
14901	AGCIAATTT	IGIATTITIA	GTAGAGATGG	CCCTCCCCC	ACCAAACTCC
14951	GAIGAICIG	AIAICHIGAC	TTCGTGATCC	CCCTACACCT	ACCAMBIGC
1200T	IGIGATIACA	GGIGIGAGCC	ACCGTGCCCG	GCCTACAGTT	GICTIIIII
T202T	ACTOACTOC	ACAGAIGAAI	CATTATAAGG	AGGI IAGCI I	ATTECCAAACT
			TTTATCAACA		
12121	TTAACACTTT	IACCIAMATI	TATAACTGAT	GCAIGIAIGC	AIAIAIACAI
15201	ACATACATAC	AIGIAIAIGI	TGTTATATAT	GIAIGGIAI	CATCAGIAIA
			TTTATCTGAA		
			כוכוכוכוכו		
15351	ATATATATAT	ATATATATAA	ATATATGTAT	ATATATTTT	TCTTTTTTG
15401	AGACAGGATC	TCATTCTGTC	ACCCAGGCTG	GAGTGCAGTG	GIGGGATCAT
15451	GGCTCACTGC	AGCCTCGACC	TCCTGGGCTC	AAGTGATCCT	CCCACCTCAA
			ACAGGGGCAT		
15551	TTTGTATTTT	TTTGTAGAGA	CAGGGTTTTG	ccrremecc	CAGGCTGGTC
15601	CTGAAATCCT	TGGCTCAAGC	AATCTGTCCA	CCTCAGCCTC	TGAAAGTGCT
			CTGCGCCCAG		
15701	AAAAAAGTAA	CCTGCTCCCT	ACTGAAGTAA	ATAGAGTTAA	AAAAAGTAAT
15751	CTGGTACAGA	CACCTGTATT	TTCTGACACC	CCTAGAAGAG	TCCCAGGTAC
15801	CCTATAATCA	AATACATTAA	CATTTCTGCA	GCAAAATGTA	TGGATAAGTG
15851	AGTTAAATAG	AGACCATGAG	TAGCTTCAGG	TCAGTTCAGA	TCAAGTTTTG
15901	CTTCTAATTA	AATGTTGATA	TTCTCTTACA	AAAACTTTGG	GTTGGGTTT
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16001	TCTTGCTGTG	TTGCTCAGGC	TGGAGTGCCA	TGGCACGATC	ACGGCTCACT
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16101	AGCTGGGACT	ACAGGAGTGT	GCCAACATGT	CCAGCTCATT	TITGIATICT
16151	TAGTAGAGAC	AGGGTTTCGC	CGTGTTGGCC	AGGCTGGTCT	CAAACTCCTG
16201	GTCTCAAGTG	ATCCGCCTGC	CTTGGCCTTC	CAAAGTGTTG	AGATTATAGG
16251	TGTCAGCCAC	TGGGCCTGGC	AGAATTATAC	ATTTATATGT	CAATATTTGC
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16401	ATTGGTCTAC	CCTAGGTTAC	TCAACCAGGC	CICCITIGIT	TAGTGAGTAG
16451	CAGGCAGTGT	TGTACAACAT	ATGTAGCATA	TCTGTATATG	TCGTCGAACA
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			GGGTATGAAC		
16601	ACATTICCAG	ATTATICTIT	AGAAAACTTG	AATCAGTTTA	TTGTGCCACC
16651	ACTICATION	пестисть	AAAACCCTAC	CAATGITIGG	TITIATITI
16701	ATTACTATT	CCTAATTICA	TAAGTACTAA	TGATATTTT	TAAAAGTAGT
			TTATAAGTCT		
16801	CTTTAGAAGC	TICCAAATICAC	CTGGCAATTA	ΤΔΤΑΤΑΛΤΑΤ	TTGAAAATAC
16851	AAGAGGACAT	ATGCCACTICA	ATATATTAGA	CLAVAVCLIC	ATTCCCATAG
16001	CTAATCAACC	AATICLITICAC	ATTATCTTAG	CCTTACATT	CTCACCTGAC
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	W-101100	~~·~~~			

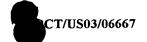


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17101	CATCCTTCAG	AGGATCAAGT	CTGCAAGAGT	ACCCATATCT	TAATCTCTTT
	CAGTIGCTATC				
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17351	GGCTCAAGTG	ATCCTCCCAC	CTCAGCCTCC	TGAGTAGCTG	GGACTACAAG
17401	TGCATGTCAC	CACATTTGGC	TAATTTTCAT	ATTTTTTGTA	GAGACGGGGT
17451	TTCGCCACAT	TGCCCAGGCT	GGTCTCAAAC	TCCTGGACTC	AAGGGATCTG
	CCTGCCTCAG				
	CCGGCTCCCC				
	TCTTGTCGCC				
17001	TECHNOCO	TECCTTCAAC	CATTO	CONTCIONOC	CCCCACTACC
T\027	TTCCACCTCC	IGGGIICAAG	GALICICE	GICICAGCCI	CCCGAGIAGC
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	TAGAAATGGG				
17801	TCAGGTGATC	CACCTGCCTC	GCCCTCCCAA	AGTGCTGGGA	TTATAGATGT
17851	GAGCCACCAT	GTCCAGCCAC	CCATTTAATT	TTTTGAGCAC	AAAATATGTA
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	TCATGAGGGG				
	CACATGCTAA				
	AATGACTTCT				
	TGTTACGAGA				
18121	CCGAGGTGAG	AGIGTAAGGC	CTGGGCAAGG	GHGGGAGGC	AGITCIAAIA
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	TCTATCCAGT				
18301	GGGGCTACTA	AGGCTAGTAA	GTAGTGAGGC	TGGATTTAAA	CTTAAGTCTC
	CAGCTTCGTG				
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18751	GAATGGGTTG	GACAGTGATG	AAGAACACAG	AAACAGCATT	GATGCCTACA
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	GCACTGAGAT				
	AAAAAAAAA				
19301	ATTITCTCTAA	TTCAGATTTG	CGTCTTCCCA	AGGGTCAAAA	TTATATTTT
	ACTATCCCTG				
	пппссп				
	CTCCTTTCAT				
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				GCTTACAGTC	
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19601 19651	ATTTATGTAT CAAGCAGATG ACTACTTCAT	TTTAAATTTA ATGTTATCTT TCACAGTTCA	AAGTATTGAC ATATATTCAC AAATGAAAAC	AGTGGTGAAA AGAGTTTAGT AGCTAATTCT	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG
19601 19651 19701	ATTTATGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT	TTTAAATTTA ATGTTATCTT TCACAGTTCA ACTCTTTAAA	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT	AGTGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT
19601 19651 19701 19751	ATTTATGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT	TTTAAATTTA ATGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT AAGTTATCTG	AGTGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTGGGACTG	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA
19601 19651 19701 19751 19801	ATTTATGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTGCACAGTT	TTTAAATTTA ATGTTATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT AAGTTATCTG TATGGACTGT	AGTGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTGGGACTG TTTTGCACAT	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA
19601 19651 19701 19751 19801	ATTTATGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT	TTTAAATTTA ATGTTATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT AAGTTATCTG TATGGACTGT	AGTGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTGGGACTG TTTTGCACAT	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA
19601 19651 19701 19751 19801 19851	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTIGCACAGTT CATTTIGAGGT	TTTAAATTTA ATGTTATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGTTAGGGG	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT AAGTTATCTG TATGGACTGT AGGAGGTGTC	AGTGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTGGGACTG TTTTGCACAT ATCTTTATGG	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA CACTTTCTGG
19601 19651 19701 19751 19801 19851 19901	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTIGCACAGTT CATTTIGAGGT CTIGGGAAGGG	TITAAATITA ATGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGTTAGGGG AGTCAGTCCT	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT AAGTTATCTG TATGGACTGT AGGAGGTGTC AATTGAGATA	AGTGGTGAAA AGAGTTTAGT AGCTAATTICT AGGAGAGCTA ACTGGGACTG TTTTGCACAT ATCTTTATGG ATAACTAGCC	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA CACTTTCTGG ACCTGGCCAC
19601 19651 19701 19751 19801 19851 19901 19951	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTIGCACAGTT CATTTIGAGGT CTIGGGAAGGG ACACAAGTIGT	TTTAAATTTA ATGTTATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGTTAGGGG AGTCAGTCCT GTTTTGCCTT	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT AAGTTATCTG TATGGACTGT AGGAGGTGTC AATTGAGATA AGTTACCTGT	AGTGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTGGGACTG TTTTGCACAT ATCTTTATGG ATAACTAGCC CACACACTGA	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA CACTTTCTGG ACCTGGCCAC GCAGTGAGAC
19601 19651 19701 19751 19801 19851 19901 19951 20001	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TIGCACAGTT CATTTGGAAGGG ACACAAGTGT TCAAGAGAGGT	TITAAATITA AIGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGTTAGGGG AGTCAGTCCT GTTTTGCCTT GTCAAAGTAC	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCTG AAGTTATCTG TATGGACTIGT AAGGAGGTGTC AATTGAGATA AGTTACCTGT TTTTCAATGC	AGTIGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTIGGGACTG TITTIGCACAT ATCTTTATIGG ATAACTAGCC CACACACTGA ATAAAGCACT	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA CACTTTCTGG ACCTGGCCAC GCAGTGAGAC ACAGATCTGT
19601 19651 19701 19751 19801 19851 19901 19951 20001 20051	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TIGCACAGTT CATTTGGAAGGG ACACAAGTGT TCAAGAGGAGGG ACACAAGTGT TCAAGAGGAGT CCACACTGTT	TITAAATITA AIGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TIGITAGGGG AGTCAGTCCT GTCAAAGTAC GTGAGTGAGC	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCTG TATGGACTIGT AAGGAGGAGTA AAGTTACCTIGT TTTTCAATIGC AGGTTGGCAC	AGTIGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTIGGACTG TITTIGCACAT ATCTTTATIGG ATAACTAGCC CACACACTGA ATAAAGCACT GGTIGCCTIGTIG	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA CACTTTCTGG ACCTGGCCAC GCAGTGAGAC ACAGATCTGT TGCGGGGGTG
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19601 19651 19701 19751 19801 19851 19901 19951 20001 20051 20101 20151	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTIGCACAGTT CATTTIGAGGT CTIGGGAAGGG ACACAGTIGT TCAAGAGAGT TCAAGAGAGT TCAAGAGAGT TIGTIGTTIGACT TTIGCTCTIGTT	TITAAATITA ATGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGITAGGGA AGTCAGTCCT GTTTTGCCTT GTCAAAGTAC GTGAGTGACC CACGTGCTGT GTGACTGAAG	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCTG TATGGACTGT AAGTGACTGT AAGTGAGATA AGTTACCTGT TTTTCAATGC AGGTTGGCAC CCTGTGATCT CCCAGCTGAA	AGTIGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTIGGGACTG TITTTGCACAT ATCTTTATGG ATAACTAGCC CACACACTGA ATAAAGCACT GGTGCCTGTG CTCAGGACTC GGTGCTGGAA	ACCTGTTCAA AACTGAGCCA TTTAAGTAAG CTATAATACT GGGTGGAATA TCATAATGGA CACTTTCTIGG ACCTGGCCAC GCAGTGAGAC ACAGATCTGT TGCGGGCGTG AGGTCCTGAA GTGCAGTGACAC
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19601 19651 19701 19751 19801 19851 19901 19951 20001 20051 20151 20201 20251	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTIGCACAGTT CATTTIGAGGT CTIGGGAAGGG ACACAGTGT TCAAGAGAGT CCACCAGTT TGTTGTTGACT TTIGCTCTGTT CCTGGAGGAA GTTGTGTAAG	TITAAATITA ATGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGITAGGGG AGTCAGTCCT GTTTTGCCTT GTCAAAGTACC GTGAGTGAGC CACGTGCTGT GTGACTGAAG GAACCAGTAA AATAGATATC	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCT AAGTTATCTG TATGGACTGT AGGAGGTGTC AATTGAGATA AGTTACCTGT TTTTCAATGC AGGTTGGCAC CCTGTGATCT CCCAGCTGAA CAGCAGAGGG TGCCGTTTTT	AGTIGGTGAAA AGAGTTTAGT AGCTAATTCT AGGAGAGCTA ACTIGGGACTG TITTTGCACAT ATCTTTATGG ATAACTAGCC CACACACTGA ATAAAGCACT GGTIGCCTTGTG CTCAGGACTC GGTGCTTGGAA TGGATGAAAG TGTAAGCCAA	ACCTIGITICAA AACTIGAGCCA TITTAAGTAAG CTATAATACT GGGTGGAATA TCATAATICGA CACITTICTIGG ACCTIGGCCAC GCAGTGGGAC ACAGATICTIGT TGCGGGCGTG AGGTCCTGAA GTGCAGTGAC GGAATTIGATA GACACCTTTA
19601 19651 19701 19751 19801 19851 19901 19951 20001 20051 20101 20251 20201 20251 20301	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTIGCACAGTT CATTTIGAGGT CTIGGGAAGGG ACACAGTGT TCAAGAGAGT CCACACTGTT TIGGTTGACT TTIGCTCTGTT CCTGGAGGAA GTTGTGTAAG CCCTTCCAGT	TITAAATITA ATGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGTTAGGGG AGTCAGTCCT GTTTTGCTAAGTAC GTGAGTGAGTCAGTGCTG GTGACTGAGTGAGG GAACCAGTAA AATAGATATC AATTGTTTCA	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCTG TATGGACTGT AGGAGGTGTC AATTGAGATA AGTTACCTGT TTTTCAATGC AGGTTGGCAC CCTGTGATCT CCCAGCTGAA CAGCAGAGGG TGCCGTTTTT TCTTTTAATA	AGTIGGTIGAAA AGAGTTTAGT AGCTAATTICT AGGAGAGCTA ACTIGGACTG TTTTTGCACAT ATCTTTATIGG ATAACTAGCC CACACACTIGA ATAAAGCACT GGTIGCCTIGTG CTCAGGACTIC GGTIGCTIGGAA TIGGATIGAAAG TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TICATTTIGGCT	ACCTIGITICAA AACTIGAGCCA TITTAAGTAAG CTATAATACT GGGTGGAATA TCATAATIGGA CACTITICTIGG ACCTIGGCCAC GCAGTGGAGC ACAGATCTGT TGCCGGGCGTG AGGTCCTGAA GTGCAGTGAC GGAATTIGATA GACACCTTTA TCATTTACAG
19601 19651 19701 19751 19801 19851 19901 19951 20001 20051 20101 20251 20201 20251 20301	ATTTATIGTAT CAAGCAGATG ACTACTTCAT TATAGATTCT ATTATAGAAT TTIGCACAGTT CATTTIGAGGT CTIGGGAAGGG ACACAGTGT TCAAGAGAGT CCACCAGTT TGTTGTTGACT TTIGCTCTGTT CCTGGAGGAA GTTGTGTAAG	TITAAATITA ATGITATCTT TCACAGTTCA ACTCTTTAAA AAGTGAAATT TATTGAGAAA TTGTTAGGGG AGTCAGTCCT GTTTTGCTAAGTAC GTGAGTGAGTCAGTGCTG GTGACTGAGTGAGG GAACCAGTAA AATAGATATC AATTGTTTCA	AAGTATTGAC ATATATTCAC AAATGAAAAC AGAGTTATCTG TATGGACTGT AGGAGGTGTC AATTGAGATA AGTTACCTGT TTTTCAATGC AGGTTGGCAC CCTGTGATCT CCCAGCTGAA CAGCAGAGGG TGCCGTTTTT TCTTTTAATA	AGTIGGTIGAAA AGAGTTTAGT AGCTAATTICT AGGAGAGCTA ACTIGGACTG TTTTTGCACAT ATCTTTATIGG ATAACTAGCC CACACACTIGA ATAAAGCACT GGTIGCCTIGTG CTCAGGACTIC GGTIGCTIGGAA TIGGATIGAAAG TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TIGTAAGCCAA TICATTTIGGCT	ACCTIGITICAA AACTIGAGCCA TITTAAGTAAG CTATAATACT GGGTGGAATA TCATAATIGGA CACTITICTIGG ACCTIGGCCAC GCAGTGGAGC ACAGATCTGT TGCCGGGCGTG AGGTCCTGAA GTGCAGTGAC GGAATTIGATA GACACCTTTA TCATTTACAG





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20451	AGTAAATATG	TTTTCTGACA	ATTATAGGGA	AGGGAAGAAA	AGGAAAGTCC
20501	AATTAAAGCA	тттстсст	CAGAGTTTGA	AAAATAGAAT	TCATGCAATC
20551	TTTTAAATTC	CATGCCAACA	CATCAGACAA	GAAGAGACTT	GATAGTAGTA
20601	AAGGTTGGGA	ATCAAAAGAA	CAATGTAAGT	TTTTGATATT	GACTTCAAAA
20651	CATGGTGTTC	TATAATTTAG	TGTTCATTTG	TTACGTGTAT	GGTATTATAA
20701	TTAATTTIGT	ATATGTGGTA	GTTATTTTTT	GTACTTTGAT	TAGGAAACAA
20751	ATATTGAGCC	acttcaagag	GCAGACTATT	TTGGAAAAAA	AAGTCTGGTA
20801	AAAGTAATGC	TTAATCTAAT	TAATCIGICT	TCATCCTCTT	AATTCATCAA
20851	GATGACTTTG	GGIGICIGGI	GGCAACTGAG	AATGGGTTAT	GGAAGAACGT
20901	CAAGGCAATG	TAATCCCTAT	TATTTACGGT	TACTTGAGAG	GATAAATTAA
20951	TCAGCGGTCA	CTAATCTTTG	GATAATCACT	CTATTGAGCT	GGAACTATCC
21001	TTAGTATTTT	GGAAAGCAAG	TCAGTGAGTT	AGAACTGTCA	AAACIGATCA
21051	GCTTTTCTAA	GCTTAATGAT	AAGIGAAIAG	AAACIAGIIG	CHICACCE
21101	TTTCCTCCCT	GCATTGCAGC	ATGAICALIC	IGIAACICIG	GAAAIGGIII
21151	ATGGAACAAC	AGTGAAAATA	CATIGATACA	CIGICIIGIG	GIAGATTIA
21201	AGATAGGCTT	TAGACAAAGI	TCAGAGCCTT	ICCICIAGCI	GGGGATTAAC
21251	AAAGCTGCCT	TCATAGITAA	AIGITIGCAC	CCIGIGIAIG	CATTICAGI
51301	TACTAGAATT	AGGIAAGI IA	GIGITATAA	ATTIGGITIGA	CATTACATAC
	TTTAGGAAGT				
	ATACATATTT				
21421	CTGGGGTGGG	IAIGGGAIA	AAGAAAGIA	TGAGGGGTCT	ATTTCAAAAT
5120T	CATGGAAAAA ATTTTTGAAC	AIGIACACIA	TUCTACTAAC	CIGIGCAIGG	ATCTCTCAAC
51501	TIGITACAAC	ATCTCTCAAC	ACTICACACAC	ATTAACAAAT	CATATOCCAC
216E1	CAGTTTTTAA	AAACCCCCTA	TCACCCTAAC	ATCAATTCTC	CTAAAATTCA
21701 21701	AGCAAGAACA	AACATCAAAT	TEATGCTGCT	CCTTCCCTAC	AAGGATGGTG
21701	AAATCATTGA	TECTTTACAA	AAACTTTATC	CCCACAATAC	TITTAAAGGAA
21/)1	CCAGCAGTTT	ACAAATIGGCT	AACATCCTTT	AAGAAGGGAC	GAGATGATGT
	TGAAGAGGAA				
	AAATTAATCT				
21951	TTAAACAAGT	GGGATTGAGA	TCCTGTGGCA	TATGTCTGAA	GGATTGTAAT
22001	AGGAGAGGAA	ACATGGCTTT	ACCAGTATGA	TGCTGAAGAC	AAAGCACAAC
22051	CAAAGCAATG	GCTACCAAGA	GGTGGAAGTG	ATCTAGTTAA	AGCAAAAGCA
22101	GACTAGTCAA	GAGCAAAGGT	CATGATAAGA	GACTITIGGG	ATGCTCAAGG
22151	TATTTTGCTT	GTTGACTTTC	TGGGGAGCCA	AAGAATGATA	ATATTTGCTT
	ATTGTGTGTG				
22251	TACCCAGGGA	AGCTTTACCA	GAGAGTCCTT	CTCCACCAGG	ACAATGTTCC
	CGGTCATCCT				
22351	AATTATTAGG	CATTCACTTA	CAGICITITI	ПППППА	GTTGGAGTCT
22401	TACTITGTCT	CCCAGGCTGG	AGIGCAGIGG	IGCAAICIIG	GCTCACTGCA
22451	ACCTCCACCT	GCCAGGTTCA	AGCAATICIC	CIGCCICAGE	CICCAAGIA
	GCTGGGATTA				
	AGTAGAGATG CCTCAGGTGA				
22651	ATGAGCCACT	CIRCUTION	TATCTTACAG	TCTTCATTTC	COTTATO
	ACTICITITI				
22751	TCTTCAGTTA	ΑΤΑΑΤΙΞΤΑΑΑ	AAGGACTIGCA	TIGACATGAT	TAAATTCCTG
					AACTCACAAA
22851	AGTATCTTGA	ACTTGATGGA	GCTTATGTTG	AGAAATGAAG	TGTATATTTT
22901	CATTATCTTT	TAATTTCATT	CTTTAGTGAA	TTTTTTGAGG	TCCCCTTGTA
22951	TACATTITAA	TCCTAAGGGA	ATAAAGAAAG	GAGGAAGTCC	TAGCCCTGTG
23001	CIGICIGCCT	AGGTACAGTG	TCTGAAACAC	AGACCAGTAT	TCACCCTTTG
	AAATTTGAGG				
	CTATGCAGGT				
23151	AATGCCATTT	TCATAACAAA	CTTCACCTGC	TTATGTACAT	TGTAAATTGT
23201	TGCCTTGATA	AGCTTCCCGG	AGATAAAGTA	ATTCAGCTAA	GTATTATTTC
23251	CAATCATAAT	THGIGICAT	TATGAGCAAC	ACAATACTAT	ATAIGGGATT
23301	GATTCACTGC	AGAACTGGAA	IAAATATAAA	TAGATCTTT	AGAAAAGAAA
23351	CGTAGATTTA	AAAATCTTAT	GTTAGAAGGC	ICAATTAATT	AAAIGIAATT
23401	AATTTTTAA	AATCAGCTTT	ATTGAGGGAT	GACTIAGATA	I IAIAIAAIT
23451	CACAAATTIT	AAGIGIACAG	ILIGATAGIT	CIGACATICA	AACTGTATAC
23501	AAICAIGIAA	CALLATCAC	AAICAIAAIA	IAGIGIGICC	ATCACCCCAG
4335L	GGIGIACCCT	MIGRICUIT	TIIGCAGIIA	ACTATACCT	CTTACATTCT
23CE1	AAAATTTAT	ATCAATCCAA	TCATACACTO	TOTAL	TGTATCTGTT
232V1	TTTCACTCAC	CATIGATICETT	TTCACATTTC	TOTTET	GGTATGTATT
23751	ACTACTOR	TCTTTTAT	TACTAAGTAG	TATTCCATTC	TATGCCTATG
, JT	, 20, 20, 10, 1				



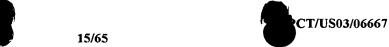


23801	CCACATTTTT	TITITITITI	TTCGAGACAG	AGTTTTGCTC	TGACATCCAG
			TCATGGCTCA		
			TCAGCCACCT		
			TITAAATIGI		
7323T	CTATATTCCC	CACCETTECTTE	TCAAACTCCT	CCCCCCCAACC	AATCCTTCTC
			GGGGTTACAA		
			ATTCACATAT		
24151	TCAGTTGTTG	CCTATTATGA	ATAGAACTGC	TATGAACATT	TGTATGCAAA
24201	ccrrreries	GATGTATGTT	TITATTICIC	TTTTGTACAT	TAAATTTAAAA
24251	TTTAAATTTT	GTTCIGIATT	ATTIGIATTI	TTAAATTTCT	CAAGTGGGTA
24301	ATACTGTGTA	CIIIIIIII	GAAATTAAAA	AAATTGTGGC	TGAACAAGGA
			AGGACTICTGG		
			GGTGCTGCCA		
			GAAAGACCAA		
			ACTTCAGCCA		
			GATTATAGTC		
			TAAGAAGGGA		
			GAAGATTAGA		
			GAGTAGCTTG		
			TGAAGTTACT		
			ATCTTTACAA		
			CAGAACCAGG		
24901	GAGCAAATGT	AGGTAGGTTT	GGTGAGGATC	AGGAAATGGA	GGGGAAGAGG
24951	TCATTAAATG	TGGTCCTGGG	GTTGAGCAGC	AGATTGGAAG	AGAATGGCAA
			GATAAGGAAA		
			TAGTGAAACT		
			CTGATAGGTG		
			AAGAAATTTC		
			TCTCATATAG		
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			ATAAAATTAC		
			TTTACCATTT		
			ATTIGITIAA		
			AAAAACCTGT		
			AAATTTTATG		
			TAAAAAAAAT		
25601	TTAACATGCA	TAATGTGATG	TTTTGTATTA	TGTATAACAT	GATGTATATG
25651	TCATACATAA	CATATATACA	TIGTAGAATT	GTTAAGTCTA	GGTAATTAAC
25701	AAATGCATTA	CCTCACACAG	TTATCATTTT	TGTGGTGAGA	ACATTTTAAC
25751	ATCCACTCTC	TTTAAATTTT	TCAAGAATAA	AATTTTATCA	TCTGGTCATG
			CAACACTTTG		
			AGACCAGTCT		
			AAAAGAATGC		
			TIGICGITAT		
			TAACCAGTCC		
			GCCTTTTAAG		
			TGTACCTGGC		
			GTGGCATTAA		
			AATTTTAATT		
			ATTCTTGATC		
2630T	TAACTGAGTA	GAATATTTT	GIATGIGIGI	ATAGATGIGT	GIGIGIGIAT
			ATATAGATAT		
			GCCCGGGGCTG		
26451	GCTCACTATA	GCCTCTACCA	TACAGGCTCA	AGCAATCCTC	TCACCTCAGC
26501	CTCCCAAGTA	GCTAGGACTA	CATGCATGCA	CCACCATGCC	TGGCTAATTA
			AGAGATGGGG		
26601	GCCTCAAACC	TCTAGGCTCA	AGCAGTCCTC	CTGCCTTGGC	CTCCCAAGGT
			CCACCGTGCC		
			CAAGTGCTGT		
			TIGTAATTAT		
			GTGCAGGGGC		
			ACAGTGCTTT		
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			ATGCTTCATA		
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			GTTTTATTT		
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2/151	TAATCCCAAA	GITTGAAGGC	TGTAGGTTAA	TTAGGATAAC	TTGACAGGAA





27201	GTGAGTTAAT	CAAATTTGAG	AGTTTAATCT	TCCAATAATT	TATGTTCAGA
27251	CATACTTCAA	GTATATCAGC	AGGTAACAGG	AACTITAGTT	GCAGAATGCC
27301	CCAAAACACA	AGAACTCCAG	TGGATTTTCT	GGCTTCCAGG	AATGTTTTGG
27351	AGGAAGAAAA	ACCAATAAAA	TGATTTGGGG	GICATTTIGI	TCCATTACTC
27401	TATATTAAAT	ATACTAGAAT	TTAAAAATATT	AAATTTTAAA	AGATAAAAAG
27451	ATGCAGTTTA	CCTATTAACA	AATTAAATAA	TTTAGGAATT	CTACTTAGTT
27501	CTGTAATACT	TTAATATGAG	TAAATATGGG	CATTTCTGTG	TTAGCTAGAA
27551	TTAGATAGAG	TATTGCCATT	TTTTCAACT	GGCTTATGGT	TAAATGGAAG
27601	TAAAGGGGCA	AACTACACAT	ATAAGAATTA	GTAGTACAAT	ATTTAATACA
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27701	TGTGTGCTTG	TGAAAAAGGC	CACTGGAGGC	CCTTTTCAAA	AATTAAATCT
27751	GCCTCCAGCA	AGGTGTTTTT	CGATCACATG	GAAAGGGGAA	GAAGAAGCTA
27801	TCAGGAGCTC	TGGGGTTTTT	THIGHTIGHT	गाजाजा	TTGCCACTTT
27851	TAACTCTCAA	GCTAAAACTG	GGGTTTCATT	TGAGGAACCA	GTAATAGAAA
27901	ATTICTIATG	TACATTCAGC	AAAATCTAGT	ACTGAGTGGT	TACTTTGGCT
27951	TTTCATTGTG	GGGATTGTGT	GIGIGIGAGT	ACATGCACGC	ACTIGIGIGI
28001	TTAAGCGTGT	AAGGCAGACA	GACAGTGGGT	ACAGGICTTT	GAAATGGACT
28051	TCTTGGCAAA	AGTAATAGAG	AAAAAGAGGA	ATACAAATAA	GGGAGGAGGG
28101	ACAGGGAAGA	GCAGAGTCAC	AGGAAACAGT	GAATGAGGCT	GCAGTCTCAG
28151	TOSCCCTTTC	THGCCCTC	CAGIGITGIT	GCCTGTCTTA	TGATGATGCT
28201	GGTTTTCAGC	CAACCTTGAG	TGAGTAAAAG	CCCGGGTCTGA	GGTCTCAGTG
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28301	GCAACAGCAC	AGATTTCCAG	GAACAGTTCC	TCTTGTCATT	HIAHICCIG
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7820T	GAACATCACT	AGITACCATT	CTCATCTCTC	ACACTTACTT	CACACCTTAA
	AGATGTTCCA				
20CE1	GAATGAAAAG	ACAAACTTCT	CANATETETE	ATCTCATCC	ATTICCTION
28701	AAAGTCATGT	AAAGCAATCC	TACCACATICT	CATAGAATCT	AAAAGGCTAT
28751	ACTGATGCTA	AGATICCACTA	TTATTTTCTG	TACACTIGAGA	AAGGGGGAAA
28801	ATTGCCACTT	AAATTGTGAT	GTAATGTCTC	ATTATGGATT	GTAAGATACA
28851	TCTACATTTT	AGAAATGGTA	TAATGTTAAA	AATATGCATT	TTAAATTGAA
	GGTAAATTTA				
28951	TGAAGCATAG	TTATGTAATA	AAAATAGAAA	AGCATGCATA	GGAATGCTAT
29001	TTAGCCAATA	CAGGATGTGG	TAATCTCTAT	AAAGGGAGGG	AGGGAAATGG
29051	AGGGGGGAGG	CCAGAGGAGG	GGCCTCATCT	CTGTAGTTTA	TTTTTAAAA
29101	TTATAAAGCA	AATATTACCA	GAGTTAAGAT	TTTACAAAAT	TCATTGGTAA
29151	GCACCTATAA	TTTCTGAGT	GCTTTCAGTA	TITICATAATG	AAAAGIATGT
29201	ATTTTAAAGG	TACGITATE	AIIIAIIIII	AIIIAIIIII	TITIGAGACAG
2925I	TGTCTCATTC	CATCGCCAG	GCIGGAGIGC	AGIGGIGA	CAAACCAACT
203E1	CTGCAACCTC	CHAVAGCIA	CCATTCTATT	TITTTAAAT	ACTATITAAT
	TGTATGTTCT				
20451	TTTTTGGTG	GAAGTGAGGA	CAGATTECTT	TICACATICTE	CATTITICIC
29501	TCTGAATTAA	AAGATGGACA	AGTATCATGT	ATTATCTTAG	TAGTCATCAA
29551	ACAAGGAAAA	AGGITICITI	GIIGCIIG	TTTTTAGA	TGAAGTCTCC
	GCCCAGGCTG				
29651	TCCTGTGTTC	AAGCAGTTCT	CTGCCTCAGC	CTCCTGAGTA	GCTGGGATTA
29701	TAGGCGCCTG	CCATCACGCC	GGCTAATTTT	TGTATTTIGA	GTAGAGACAA
	GGTTTTGCCA				
	CCACCTGCCT				
29851	TGCCCGGCCCT	GGAAAAAGTT	TTTAATGGTA	AAGATGTCAT	GGAATGAATA
29901	GGATTGGCTG	GCATTATTTC	TIGCIGITAA	TAAGCAGTGA	GAAATGTTTC
29951	CATTATATGT	TTCTTTGAAG	CCAGCITICI	GGTTGCTCCC	TTATTCTTTC
30001	TTTCTCAGGC	ATGIGGIATC	TAGAAAGGGT	CAGGAGTACC	TTGATAAAAA
3002T	TTATTGTACA	AGI IGAGCAA	ACCICAGIAG	ACCTACCAA	AGAGAICIGA
30121 2010T	TAAAGAGGCA TTAACCCCTT	TACTICAAACC	TAAAAACACC	TOTOCACTET	
	TCACCAGATG				
3020T	GGAATCAAAG	CACTICAACCC	CIGITICITY	TATCATACTA	CTTGTAGGGA
30201	CCCCTTACCT	CCTATACCCA	TGAAAAAGGA	ATATTICTTA	TATCCCATAA
30351	TATTCTTTA	GTATCACACT	TAGGITITAA	והוכוד	GTTAGAGTAA
30401	AATAATTIGG	GCAAGACCAA	TTTTTAAAT	GGCAAATATA	GTCACATCAC
30451	TTGATTCACA	ATCTCACTCC	CTAGCATCTC	GCGTAATGAC	TCATAAGAAA
30501	GAAAAAGCTA	AATGCATGAA	GAGGTTCACT	ATACCATTAC	TATAAAAAAG
30551	TAAAAATTTG	TTTTGTTAT	пппп	TTTTTGAGA	TGTAGTCTCT
			_	_	



30601	CTCTGTTGCC	CAGGCTGGAG	TGCAGTGGCG	CAATCTCGGC	TCACTGAAAC
			CAATTCTCAT		
			ACCATGCCTG		
			GTTGGCCAGG		
30001	TOACCTGATC	CACCCACCTC	AGCCTCCCAA	ACTICCTICCO	TTACAGGCAT
			AAAAAGTAAA		
			TTAAATGCTG		
			ATGGTTACTG		
			ACATGACTGT		
31051	TGTGAGGAGA	GATCAAGGGA	ATATAGAAAA	ATGAAGACAT	AGTTGTGTTA
31101	GGGTGGTAGA	ATTITIGAGTG	GATTTCTCCC	CCCACTATTG	GTAAAAATTT
31151	TTGTACTTAA	TTCGTTGTGG	GCAGCCAGAT	CTTTTAAAGG	TAAATTTGAA
			AGACAGAAGG		
			AGATAAAACT		
			TIGATIATIT		
			ATGGAAGTTG		
			GCCAGGTGTG		
			GTGGGTGGAT		
			GAAACCCCCGT		
31551	AAATTAGCCC	AGCATGGTGT	TGGGTGCCTG	TAGTCCCAGC	TACTTGGGAG
31601	GCTGAGGCAG	GAGAATGGCG	TGAACCCGGG	AGGCGGAGGT	TGCAGTGAGC
31651	CCAGATCAAG	CCACTGCACT	CCATCCTGGG	CGACAGAGCG	AGACTCCGTC
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			ACCAAATAAA		
			TATTIGCITI		
			AGAGCCAAAG		
			TTGAATAGAA		
			TATACTTCTT		
			AACCCCACAG		
			ATAGAATTCA		
32101	AGAGAATAGA	AAAACTAATA	GACTGTAAGA	ATTTTAGACC	TCTGTGGCCT
32151	TGCTGAACAA	TTAATCCAGC	CCCTTCACTT	TACAGGTAAG	TAAACAAGTC
			CTGTGTCTTA		
			GAGAACTGGA		
			TTTTAAGAAA		
			ATAGAATTTT		
			ACGAACAGGC		
			ACAACATAAT		
			AGAAAACATT		
			CTICTIGITG		
			AAAAATGAAT		
32651	TATAACCCGC	TCAATAAATT	TTCTGAAAGT	TATAGTAGTT	TTAAACCTCT
32701	TTTTATTCAT	TCCCTCCAGT	TCTGTCTAGC	ACCTGTAAAG	ATGAATTATT
32751	GGCTGGGTGT	GGTGGCTCAC	GCCTGTAATC	CCAGAACTTT	GGGAGGCCGA
32801	GGCGGGGGA	TCACGAGGTG	AAGAGATCAA	GACCATCCTG	GCCAACATGG
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			ACTTGGGAGG		
			GCAGTGAGCC		
			CCTCCGTCTC		
			TATATGGCAT		
			CAGTTGAGAA		
			CACAACCAGA		
			TATTCAGAAG		
			AACAGTCAAA		
33301	CTGCACAGTC	ACTGGAAGGT	GTCATGCTGA	AGAAGGCAGG	GATGGGACTT
33351	TGAAATGAGG	CCAAGTGCAT	TTCAGTAACT	GAGTGGGTTA	TCIGITGITG
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			GGTAAAAGTG		
			AGGTGAGTCA		
			CAAGAATTGG		
			AGAGTAGGCT		
			TAAACAAATG		
			ATTGGAATCT		
			TTCCAACCAT		
			AAAATGAGCA		
33901	AGGGCACATT	GTGCTGATCT	TTACTCTATA	GCATCACTGC	CAGTAGAAAT
			TGGACTGAAT		
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37401	AGATCAGCAT	GATCTTGGAG	CCTAATGTGA	TCTGGATCTT	ATTACCATGT
37451	ATGITTITAT	CGTCAGGTGC	TGCTTTGGAC	TCTGGCCCAT	TCCTCCCACC
37501	TGTCTTCATC	CTGTCGGGGT	TGATCTCTGC	CTGGTTCCAT	AGTCACTTGG
	CTTTTGGAGT				
	TATAATTCTC				
	TAGCTCAGGT				
37701	GGGTAAAAGA	ATCCATTCCC	TTTCAACCTC	TCATTACTTA	CTGAATCAAT
	TATITATITA				
37801	TACCTCTGAG	ACTGTGGCTC	CCTCTAGACA	AGGGTCTTTG	TCTGGTATTA
37851	GTCCACTTCC	TCAGTGTCTA	ATTTCATGAG	GACAGAATCA	GGGCAAGACC
	TACTGGCTAA				
37951	CCTTGAGCCA	GGAGGTGACA	GTATCTTTIG	TGTTCCAAGT	CAGATAACCA
38001	GTAACAGTAA	TATTCTGATG	TAGGTCTAAG	GGGCAATAGG	AGCCTGAATC
38051	TGAGCCCCTT	GGCAGGGATG	GTTTCCCTGG	GTTACTGGAT	TTGAGTCTTT
38101	GTCTTCCGTA	ATAGTAACTT	CTGTGACCCCT	TGGCTCAAGG	AGTCCTTTCT
38151	AACCTAAATG	CCCTCCTGAA	GAAAGTGCTG	ATATTCATCA	GAAAAAAAAG
38201	TAGGGTTTGT	GTTATGTTAC	CATCTGGGAG	ACATTGGCTT	TAATCCTCTC
	CCCTCTTCTT				
	AATCCTGGAT				
	GGGTCTTGTG				
	GGAGCAAACC				
	GGATGATTTC				
	GGCTTTTTGA				
	ATAGAAATAT				
	AACCAAATTA				
	TATAGTTAAA				
	AGAGTGATTT				
	GGCTGGAGTG				
	CTACAGGCGT				
	ATGAGATITT				
	CCATCTGCCC				
	ACCATGCCCA				
	TCTGGCTTAG				
	TAATCTTTAG				
	TACAGACTTT				
39201	GITGITCIT	CCTACCTCTG	CATTTTCATC	TATTGATAAC	TGTCAGAGTT
39251	CAAGGTCAGT	TAATTGTACA	TTTTCTGGGA	GTTTTCTCA	CTGTTAATTA
	GTAAGACTTT				
	AAGACAGTCA				
	CAACTAGGAA				
	TATTTAAACC				
	ATCTCAGTAG				
	TCTTTCTGCA				
	GCAGCATTAT ATGGGAGTGG				
20701	AAATGCATAT	CCCCCTCCAC	TECTTATEAC	TTACCTCCTC	ATCAAATTTC
30751	TGGAAAGGTG	ATCCCCAAAA	CCAGGACACA	TITATICATA	GATATAACAC
	CITACCATAA				
	CCAAAAAACT				
	TECCTICIGIT				
	TTGGATTTTT				
	TGAATATCCA				
40051	CCTTTCAATT	GCTATATAAA	AAATGTAAAG	TCIGTTTACT	GCCTTAAACC
40101	TTCTGGTGTA	TTTTTATATA	AAGTAACACC	CTTAATTCTA	ACTTGGCCAA
	CAGGTAGGAT				
	GGCTCAGATT				
	AAGCCTAAAT				
40301	ATACTGATTT	CTGTTGTAAA	TTCTTAGAGA	AGACAGACAT	AGAAATTAGT
	AACTTGAGTC				
	TGGTATATGT				
	ATCGATAGTG				
	AGGAATTATC GCTTAAAACA				
	AGTITITAC				
	TGGTGTTTGG				
40701	GTATTTATGG	ATCCTCTTT	TCACACTAAT	CTTTCATTA	CHICIIG
40751	ATAGTTCATG	CTIGTACAGT	TGCAGCTGAA	TGGTAAGTAG	GTAGAAATAT
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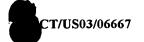






40801	GCATTGACTA	ATGTTGAACT	ATATCTAGGA	GCGTCATATT	CATGCTACTA
40851	CTGAGCACTG	TGACCTAGGT	GAAGTGTGAG	ATTAAAGAGC	TTTATTGCTT
40901	ACCACGTTTC	TTTTGATCT	AGTTAGAGTC	ATGTGAGGCA	GTCCATGACT
40951	TTTAGGATGT	TATAATATAA	TCCACATAGT	ACTITATACT	TTTCAATTTG
41001	TTTTTATATA	TTTTTCCTTA	CTATAAGCCT	GTCAAGTCTA	GTGAGATGAC
41051	ATGGTTATTA	ATATATTACA	AATGAAGAAC	TCTGACTTGG	AGGTAGTATA
41101	GCACTGTGGT	TAATAATAGA	AGTTCTTATA	TTTTTATATG	AATTATATAT
41151	TATGAACCAG	ACCAGAATAC	TAGCTCTACC	AATTACCTAG	CTGAGTGATG
41201	GTGCAGCAAC	TTAATCTCTC	AAAGCCCTTGG	TTTTCTCATT	GTAAAATGGA
41251	GGACCTTATA	GGATTGTTGG	GTAGCTTAAA	TGAGATAATA	GGTAGAATTA
41301	AAAGTAACGG	CAAAAACCGC	AATTACTTTT	GCACCAACCT	GATATTTAGA
41351	ACAGTGGAGG	CATATAGTAG	GCATTCAATA	AATATTGGTA	GTATTATTTT
41401	CAGAGGTTAT	TACTCATTTA	ACTCAACAAA	AATTGAGAGC	CCCTTTCTAT
41451	ACGCTAGTCA	TTGTGCTAGG	CATCAGGAGC	ACAGGGCAAA	CCTGGTAGGG
41501	TGCTTACTCT	GATGGAATTT	ACATTTTAGT	GGTAGAAATG	GTAAATGAGT
41551	CAACAAGAAT	TTTATGGAGT	GACAAGGACT	TTGAGGAAAG	TAAAACGGGA
41601	CAATGCTTGA	GAAGGGTGCT	AGTTGGGAAG	TCCTATCACA	CGAAGTGGTA
			ACCATAGCCA		
41701	ACTTCCCAGG	AGGAAACAGA	AGCACAGAAG	CCGAAAGGCA	GGATCACAGG
41751	CGGCACATTT	TATTGGTGCA	GTGTGGAGGT	AGAGGGACTG	GATTGTGTAG
41801	GGTTTGTAGG	CCAGGGTAAA	GAGCTTGGAT	TICTICIGAG	TGTAGGATTT
41851	TGAGCAGGGG	AGTGATGTGT	CTTATTTTGG	GCGGGGGCTA	GGCCAGGTAC
41901	TGTGAAGGAA	ATAATGGIAT	AGAAGAAATA	IGICITICII	GCIAGAAICI
41951	TATGTGACAT	ACAACTAGIG	GTGGCTGATC	AGCAATTAGA	ACIGCAGIGI
			TCTGATCATT		
42051	TTTTGCAGCA	GICAICICIA	AAGTGGCATT	AIGGIICIAG	CTCCAAACAC
42101	TIGGATCIGI	TIGCICIAAC	AGTCCGAAGG	CTAAACACTA	CACACAAAAT
42151	AGTAGAGGGA	AATGGGTGAA	AAGGCTATTT GGTTAGGAGA	CIAAACACIA	TOCTOTTOTO
42201	AACCTCCCTC	CACTECCTIC	AAACTGTGGC TCTTCCCTAT	TCACCAACCT	CAATTCCACCC
423UL	CCAATCCAAC	ATTACTICATIO	CCTTTGCTCT	CACCCTTTAC	ACTIGITAGIA
42331	CCTTTTCTCC	TOTALIGUIG	GGCCAAAAGG	CCCACTICATA	CCTTGAATT
			CATTTCCTTG		
42501	TITCICICAG	TTTAACTGTT	ATCATCAATT	GGTTAGCATT	CTAATAATAA
42551	TTATAATTAT	ACTAMACATT	TATTGAGTGC	TTACGAAGAG	CCAGTTCCAA
42601	GCTTTTTAT	CTCCATTATT	CTGCTACTTT	CCITCICATI	TTACAGATGA
42651	GGAAAATGAG	GCACAGAGTG	GTTAATTAAT	CTGTTTGAGG	TCCCGTAGCA
42701	GCTCAGTGAT	GCCAGGGTTC	AAACCTACAC	TTAACTCTAC	ACTAGAGACT
42751	GTITICITAA	TTATTICTIC	ACAATCATAT	GTTTAATGAT	TACTTATTGA
42801	TTATTTAGIG	GTCTGATAAG	AAGAGGGAGC	GGTGCTCTTC	TGTTGGAGAA
42851	GAAAGGCTGG	CTGATCAAGA	CACACTGGTT	GGTTTGAAGA	AAAAATATAG
42901	ATGTTAATTC	CATAACACCA	CACTCTAAAC	ATTICTACTG	GACGAGTTCC
42951	ACCTGTGTGC	CACTCGAAGT	CGGATGCAGT	AAGGAAGGCT	TTTTATTGAG
43001	GAGAGAACGA	ATACCTCTGT	ATTCAAAAGA	GAGTGTGTTG	TTCCTTATAG
43051	AAGATGGAAG	GGGGCTTGCC	AGTGACAGAT	TATGATGATT	ACCTCCTTAG
43101	TGGTTTTT	TTATTGCACA	GACTATAATA	ATAATTATAA	AAATTTGTAA
			CAACAAATTG		
43201	ATATTTTTC	ATATTCATTT	TATTTTTCA	TATTCAAAAA	TAAAACAATT
43251	TTCATATTCA	TITCAATIGI	TTATTTTTC	ATATTCAAAA	ATAMACAAT
			TTTTATTTTT		
			AGTTATAGAG		
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43451	AAAAGGAAAA	GACTGAAACA	TGAAAAGGTT	ACGAGGCATT	ACIAATIGAT
435UL	IGGAAIGAIG	CCIACCAGGC	AGCCCATGTC	AGITTIGGAG	CIGGULIIGG
43331 43001	AAGGAACAGC	IGIGIATTIG	GACCTTGGAG	CCCACAACTC	CAAAACTACA
436UL	AAAGIGGGCA	AAGAAGGAAG	GGGGGTTGGG AACTATCAAG	GGCACAGIG	TCACTCTTAC
4303L	GIGGITIGGA	ACIGAIGIGA	ATTICTACCT	CATATCCTAC	TTTAATTCAC
			GCAATGCATT		
			GCTTTATATT		
420C1	CCCACTTT	TEACTEAAAC	AACAAAGTTC	TTCACAAATC	CTATTTTACT
43001 4300T	CATAAACCTC	TTATTCTCTA	TITAAATICA	CITTAACTCA	AVCILCATION
430E1	TAACTTITAC	ATTICICIA	CTGTAGACTA	CCATATOO	ATTCAAACCC
40001	CTCCAACATA	TAACTICACA	CACTCTTAGG	ATGGAATCC	ΔΤΔΤΤΓΔΩΔΑ
44051	TCTTTACTCA	CAGCTTCCCA	TATCCAAATT	CCTTTTCTC	TCTTCCCC
44101	CTCCCTCTCA	CAACGCACAA	CTTGAGTGAA	ACCCCACACC	ΔΟΔΔΑΘΤΔΘΔ
44151	CATCCTCTTA	AATCTCAATG	CAGAAGGCCT	GAGACAACTIC	ATAGAGACAA
	JAI JOLIGI IA	, ~, ~, ~, ~,			





44201 TIGITICICT TITICICCCTC ATAAAATAAG	TAAAATTCAA AGTGATTTTT
44251 TTTTAATTIT TIGCTTIGAC ACATIGTGTT	TAGTCTGATT GAGGTCATCT
44301 TACACAACAG AATCCAAAAT CCTGAGAAAA	
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44501 CTGCTCCCTG CCACACTTTA TCATAACAAA	
44551 TACTIGTAGCA TIGTATAGTCA TIGGIGAATIGT	
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44701 AGAAGACAGC TGAGATGGTC TTCAGTGAAT	CIGITICACIG ACATGITIGCT
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44901 GCTTCCTTGT GGCTTGGTAG CATTACCTCT	GCATTACATG CTGCAGCCTC
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49351 ACAGCCAGTC	actagatact	TCTCCCAGCC	ACTAAGTTGT	GACTGGGGAA
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50201 TACAAGGTTT	CAAACCAAA	GGCTCAGCTC	TGCTCACAGC	AGAGGGCTAT
50251 TTATCCCTAA	ATACTTAGGG	CTAAAATTAT	CCAAAGGCAC	CAGGGCCCTC
50301 AGTGAGGAAT	GTATCCAGCC	TATACTGGCT	TATCCTTATC	CCAAAACCCCT
50351 AAAACAACTA	AGAAGGTTCC	TTGGCATAAT	AGGCATAACA	GGCATAACAG
50401 GTTTCTGCTG	AATATGGATT	CCCAAGTACG	GCAAAATAGC	CAGACCATTA
50451 TATACACTAA	TTAAGGAAAC	TCAGAAAGCC	AATACCCATT	TAGTAAGATG
50501 GACACCTGAA	GCAGAGGCAG	CTTTCCAGGC	CGTAAAGAAC	ACCCTAACCC
50551 AAGCCCCAGT	GTTAAGCTTG	CCAGCGGGGC	AAGACTTTTC	TTTCTATGTC
50601 ACAGAAAAA	TAGGAATAGC	TCTAGGAGTC	CTTACACAGG	TCCGAGGGAC
50651 CAGCTTGCAA	CCCATGGCAT	ACCTGAGTAA	GGAAATTGAT	GTAGTGGCAA
50701 AGGGTTGGCC	TCATTGTTTA	CGGGTAGTGG	CGGCAGTAGC	AGTCTTAGTA
50751 TCTGAAGCAG	TTAAAATAAT	ACAAGGAAGA	GATCTTACTG	TGTGAACCTC
50801 TCATGATGTG	AACCGCATAC	TCACTGCTAA	AGAAGACTGG	TGGCTGTCAG
50851 ACAACTGTTT	GCTTAAATAT	CAGGCTCTAT	TACTTGAAGG	GCCAGTGCTG
50901 TGACTGCGCA 50951 TGAAGAAAAG	CTIGIGCAAC	ICITAACOCA	GCGACATTTC	TICAGACAA
	ALDE-DAK MAA	ALIGICAACA	MUIAAHIGCI	WALLIAGO





E1001					
		GGACCTTCTA			
51051	TTGTATACTG	ATGAAAGTTC	CTTTGTAGAA	AAAGGACTTC	GAAAAGCAGA
51101	GTGTGTAGTG	GTCAGTGATA	ATGGAATACT	TGAAAGTAAT	CCTCTGACTC
51151	CAGGAACTAG	TGCTCAGCTG	GCAGAACTAA	TAGCCCTCAC	TCAGGCACTA
		AAGGAAAAAG			
		CTCCATGCTC			
		GGGAACCCCT			
		CACAGAAATC			
		AGAAATAAAA			
		GGCGGGACCC			
		AATCCCCTCC			
51551	AAATAGAATG	GGAAACCTTCA	TGAGGACGTA	GTTCCTCCT	CAGGATGGCT
		GAAGGAAAAA			
51651	TACTTAAAAC	CCTTCACTTA	GGCATTGATA	GCACCCATCA	GATGGCCAAA
		CTGGACCAGG			
		GTGTGCCAAA			
		GAATCTTTAA			
		AAGCTACAAA			
		AATCTACOGC			
		ATGATATCAA			
		GTTGCACCAG			
		CCAATAGTAC			
52101	GAGACAGGAC	TAGCTGGATT	TCCTAGGCCG	ACTAAGAATC	CCTAAGCCTA
52151	GCTGGGAAGG	TGACTGCATC	CACCTTTAAA	CACGGGGCTT	GCAACGTAGC
52201	TCACACCCGA	CCAATGAGGT	AGTAAAGAGA	GCTCACTAAA	ATGCTAATTA
		GGAAGTAAAG			
		GACAATGATC			
52351	ACCCCTACCC	TCTTTGGGTA	CCTCCCTTT	CTATCCCACC	TOTALLICA
52331	CTCTATTAAA	TCTTGCAACT	CCACAAAAAC	CAAACCAAAC	CAAACCAAAC
		ACAGTGACTG			
		ACTITITIC			
		GGAATTCAGA			
		GGGTAGTTAG			
52651	TACAAGATAA	AGAACTAAAA	CTAGAATCTG	GTCTTTGAAC	CCCTGGCCTG
52701	ATTGTCTTAT	TCATCATGAT	GATTTGCCTA	TTTTTCCAAT	TTCTAAATCA
52751	TTCCTCTGCT	GTTGACAAAG	CAATAAATTG	TTATATTTGA	TAAGTGAATC
52801	TTCAGAGAAC	TGGCCTTGAG	CCAGCTCTAC	AACTAACCAG	CTCTGTGGCC
		TTTCTTAATA			
	ATGAAGTTAG	16 6 16 6 6 16-1			
	ATGAAGTTAG				
52951	ATGTATATGT	ACAAACCACT	TAGTCCTGTG	CTTGGCCTAT	TIGGIGCTIT
52951 53001	ATGTATATGT TTTTTTTCT	ACAAACCACT TTTTTTTAAG	TAGTCCTGTG ACAGGGTCTT	CTTGGCCTAT GCTTGAATCT	TIGGIGCTIT TGCIGAGGCT
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52951 53001 53051 53101 53151 53201 53351 533601 53551 53601 53651 53701 53851 53801 53851 53801	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTTT TATGTATATA GITACATAGC AAGTGAGCAT TCCATCAGGC TCCCTTTCCT TTTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTTTT	ACAAACCACT TTTTTTTAAG TCCGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TTCACCCATA TCACCATA TCACCATA TCACCATA TCACCATA TCACCATA TCACCATA TCACCATA TCTCCTGCT CTGTGAAAAA TTTGAAGAGT GTTACTGCAA TTTCTTTTTT GGCGTGATCT CCCTGCCTCA TCCAGCTTAAT TCAGGATGGTC AAAGTGCTGG	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCA TCCTCCAAAA TCACCTATAT ACACCTATAT AATTATTAAC AAGACATGAC TATTTTTGGCC TGAGACAGCA CGGCTCACTG GCCTCCTGAG TTTTTTTTTT	CTTIGGCCTAT GCTTGAATCT CCTGCCTCAG CTGGTGGCAG CTTCTGACAG GCGAGAGAGG GCTGAATTCA AGITCTAGAAT AGATACTTTT TTTCTTCTTC ACAGAATAGT AGITCTATTA CTTATTCTTT CTTTTTCAGA TCTCGCTCTG CACCCTCTTGC TAGCTGGGAC TTAGTAGAGA ATGAGCCACC	TTGGTGCTTT TGCTGAGGCT CCTTCCAAGT TGCTCGTTGA TTTTGGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGTG CCCTCTCCAT TTCTTTTTT ACAAAAACAT AGAAACAATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT CTCCTGGGTT TACAGGCGGG CTGGGTTTCA ACGCCCAGCC ACGCCCAGCC
52951 53001 53051 53101 53151 53201 53351 533601 53451 53501 53651 53701 53751 53801 53851 53901 53951	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTTT TATGTATATA GITACATAGC AAGTGAGCAT TCCATCAGGC TCCCTTTCCT TTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTCT CAGAGATCTT GGAGTTCAGT CAGTGATTC TGCCACCACA TCATGTTGGC TCGGCCCCCA GATCTTGTTC	ACAAACCACT TTTTTTAAG TCCGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TTCACCATA TCACATACTG TCTCCCTGCT CTGTGAAAAA TTTGAAGAGT GTTACTGCAA TTTCTTTTTT GGCGTGATCT CCCTGCCTCA TCCAGCTAAT CAGGATGGTC AAAGTGCTGG TTTCTTTATGA	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCA TCCTCCAAAA TCACCTATCT GGCTTTTTT CAACCTATAT AATTATTAAC AAGACATGAC TATTTTTGGCC TGAGACAGCA CGGCTCACTG GCCTCCTGAG TTTTTTTTTT	CTTIGGCCTAT GCTTGAATCT CCTGCCTCAG CTGGTGGCAG CTTCTGACAG GCGAGAGAGG GCTGAATTCA AGGTCTAGAAT AGATACTTTT TTTCTTCTTC ACAGAATAGT AGTCTTATTA CTTATTTCTTT CTTTTTCAGA TCTTGCTCTG CACCCTCTGC TAGCTGGGAC TTAGTAGAGA ATGAGCCACC TTCCATGGTA	TTGGTGCTTT TGCTGAGGCT CCTTCCAAGT TGCTCGTTGA TTTTGGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGTG CCCTCTCCAT TTCTTTTTT ACAAAAACAT AGAAACAATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT CTCCTGGGTT TACAGGCGGG CTGGGTTTCA TCTGCCTGCC ACGCCCAGCC TATATGTACC
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52951 53001 53051 53101 53151 53201 53251 53351 53401 53551 53601 53751 53801 53851 53801 53951 53951 53951 54001 54051	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTTT TATGTATATA GTTACATAGC AAGTGAGCAT TCCATCAGGC TCCCTTTCCT TTTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTTTT	ACAAACCACT TTTTTTAAG TCCGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TTCACCCATA TCACCATACTG TCTCCCTGCT CTGTGAAAAA TTTGAAGAGT GTTACTGCAA TTTCTTTTTT GGCGTGATCT CCCTGCCTCA TCCAGCTAAT CAGGATGGTC AAAGTGCTGC TCAGCTTCAT CAGGATGGTC AAAGTGCTGG TTTCTTATGA TATGCATTCT GTGAACAGTG	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCA TCCTCCAAAA CTTTACACAA TGACCTTCTT CACCTTATT CAACCTATAT AATTATTAAC AAGACATGAC TATTTTGGCC TGAGACAGCA CGCTCACTG GCCTCCTGAG TTTTTTTTTT	CTTIGGCCTAT GCTTGAATCT CCTGCCTCAG CTGGTGGCAG CTTCTGACAG GCGAGAGAGG GCTGAATTCA AGITCTAGAAT AGATACTTTT TTTCTTCTTC ACAGAATAGT AGITCTTATTA CTTATTCTTT CTTTTCAGA TCTGGCTCTG CACCCTCTGC TAGCTGGGAC TTAGTAGAGA ATGAGCCACC TTCCATGGTA GCCATCTAGG CATTCACGTG CACCTCTAGC CACCTCTGC TAGCTGGGAC TTCCATGGTA AGCCACC CTTCCATGGTA GCCATCTAGG CATTCACGTG CATTCACG CATTCACGTG CATTCACGTG CATTCACGTG CATTCACGTG CATTCACGTG CATTCACG CATTCACC CATTCACC CATTCACC CATTCACG CATTCACC CATTCACC CATTCACC CATTCACC CATTCACC CATTCACC CATTCAC	TTGGTGCTTT TGCTGAGGCT CCTTCCAAGT TGCTCGTTGA TTTTTGGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGTG CCCTCTCCAT TTCTTTTTT ACAAAAACAT AGAAACAATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT CTCCTGGGTT TACAGGCGCG CTGGGTTTCA TCTGCCTGCC ACGCCCAGCC TATATGTACC TTGATTCCAT CATGTGTCTT
52951 53001 53051 53151 53201 53251 53251 53351 53451 53501 53551 53601 53751 53851 53801 53951 53951 53951 54051 54051	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTT TATGTATATA GTTACATAGC AAGTGAGCAT TCCATCAGGC TCCCTTTCCT TTTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTTTT	ACAAACCACT TTTTTTAAG TCCGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TTCACCCATA TCACCATACTG TCTCCCTGCT CTGTGAAAAA TTTGAAGAGT GTTACTGCAA TTTCTTTTTT GGCGTGATCT CCCTGCCTCA TCCAGCTAAT CAGGATGGTC AAAGTGCTGC TCAGCTTCAT CAGGATGGTC AAAGTGCTGC TTCTTTTTT GTGAACAGTG TTCTTTATGA TATGCATTCT GTGAACAGTG TGCTTTATTAT	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCA TCCTCCAAAA CTTTACACAA TGACCTTCTT CACCTTATT CAACCTATAT AATTATTAAC AAGACATGAC TATTTTGGCC TGAGACAGCA CGGCTCACTG GCCTCCTGAG TTTTTTTTAATTACAGGC TCATTATTT TCAATCTCTT AATTACAGGC CTGTTAGTA ATCATTGATG ATCATTGATG CTGCAGTGAA TCCTCTGGGT	CTTIGGCCTAT GCTTGAATCT CCTGCCTCAG CTGGTGGCAG CTTCTGACAG GCGAGAGAGG GCTGAATTCA AGICTAGAAT AGATACTTTT TTTCTTCTTC ACAGAATAGT AGICTAGTAT AGICTTATTA CTTATTCTTT CTTTTCAGA TCTGGCTCTG CACCCTCTGC TAGCTGGGAC TTAGTAGAGA ATGAGCCACC TTCCATGGTA GCCATCTAGG CATTCACGTG AGCATCTAGG ATATGCTCAG ATATGCTCAG	TIGGIGCTIT TGCIGAGGCT CCTTCCAAGT TGCTCGTTGA TITTIGGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGIG CCCTCTCCAT TTCTTTTTT ACAAAAACAT AGAAACAATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT CTCCTGGGTT TACAGGCGCG CTGGGTTTCA TCTGCCTGCC ACGCCCAGCC TATATIGTACC TTGATTCCAT CATGIGTCTT TAATAGGATT
52951 53001 53051 53151 53201 53251 53251 53351 53451 53451 53501 53651 53761 53761 53851 53801 53851 53801 53851 53801 53451 53451 53401 53451 53401 53451	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTT TATGTATATA GTTACATAGC AAGTGAGCAT TCCATCAGGC TCCCTTTCT TTTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTTTT	ACAAACCACT TTTTTTAAG TCCGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TTCACCATACTG TCTCCCTGCT CTGTGAAAAA TTTGAAGAGT GTTACTGCAA TTTCTTTTTT GGCGTGATCT CCCTGCCTCA TCCAGCTAAT CAGGATGGTC AAAGTGCTGC TTTCTTTTTT CAGGATGATCT CAGGATGGTC AAAGTGCTGC TTTCTTTTTTTTTT	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCA TCCTCCAAAA CTTTACACAA TGACCTTCTT CAACCTATAT AATTATTAAC AAGACATGAC TATTTTGGCC TGAGACAGCA CGGCTCACTG GCCTCCTGAG TTTTTTATTT TCAATCTCTT AATTACAGGC CTGTGTAGTA ATCACTGTGAGA TCCTCTGGGT TTCACTTGAG TCTCTTGGGT TTCACTTGAGT TTCACTTGATG CTGCAGTGAA TCCTCTGGGT TTCTTTAGC	CTTIGGCCTAT GCTTIGAATICT CCTIGCCTCAG CTIGGTGGCAG CTTCTIGACAG GCGAGAGAGG GCTGAATTCA AGICTAGAAT AGATACTTTT TTTCTTCTTC ACAGAATAGT AGICTIATTA CTTATTCTTT CTTTTTCAGA TCTTGGCTCTIG CACCCTCTGC TAGCTGGGAC TTAGTAGAGA ATGAGCCACC TTCCATTGGTA AGCATCTAGG CATTCACTTGGTA TCCATTGGTA ATTTAGTAGAGA ATGAGCCACC TTCCATTGGTA ACGCATCTTAGG CATTCACTTTAGG ATATTGCTCAG TCTTTGAGGA TCTTTGAGGA TCTTTGAGGA	TIGGIGCTIT TGCIGAGGCT CCTTCCAAGT TGCTCGTTGA TITTIGGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGIG CCCTCTCCAT TTCTTTTTT ACAAAAACAT AGAACAATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT TACAGGCGCG CTGGGTTTCA TCTGCCTGCC ACGCCCAGCC TATATGTACC TTGATTCCAT CATGTGTCTT TAATAGGATT TACTGCTTTC TTAATAGGATT TACTGCTTTC
52951 53001 53051 53151 53201 53251 53251 53351 53451 53451 53501 53651 53601 53751 53801 53851 53801 53851 53901 54051 54051 54051 54151 54201	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTT TATGTATATA GTTACATAGC AAGTGAGCAT TCCATCAGGC TCCCTTTCT TTTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTTTT	ACAAACCACT TTTTTTAAG TCGGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TTCACCCATA TCACCATACTG TCTCCCTGCT CTGTGAAAAA TTTGAAGAGT GTTACTGCAA TTTCTTTTTT GGGTGATCT CCCTGCCTCA TCCAGCTAAT CAGATGGTC AAAGTGCTGG TTTCTTATGA TATTGCATTCT GTGAACAGTG TGCTTTATTAT TATTGCATTCT GTGAACAGTG TGCTTTATTAT ATTGGTAGTTC GAACTAACTT	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCA TCCTCCAAAA CTTTACACAA TGACCTTCTT GGCTTGTTTT CAACCTATAT AATTATTAAC AAGACATGAC TATTTTTGGCC TGAGACAGCA CGCTCCTGAG TTTTTTATTT TCAATCTCTT AATTACAGGC CTGTGTAGTA ATCATTGATG CTGCAGTGAA TCCTCTGGGT TTCTTTTAGC ACACTCATAC	CTTIGGCTAT GCTTGAATCT CCTGCCTCAG CTGGTGGCAG CTTCTGACAG GCGAGAGAGG GCTGAATTCA AGICTAGAAT AGATACTTT TTTCTTCTTC ACAGAATAGT AGICTAGTAT AGICTAGTAT AGICTTATTA CTTATTCTTT CTTTTTCAGA TCTGGCTCTG CACCCTCTGC TAGCTGGGAC TTAGTAGAGA ATGAGCCACC TTCCATGGTA GCCATCTAGG CATTCACGTG ATATGCTCAG TCTTTGAGA ATGAGCACC AT	TIGGIGCTIT TGCIGAGGCT CCTTCCAAGT TGCTCGTTGA TITTIGGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGIG CCCTCTCCAT TTCTTTTTT ACAAAAACATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT CTCCTGGGTT TACAGGCGCG CTGGGTTTCA TCTGCCTGCC ACGCCCACC CATATGTACC TTGATTCCAT CATGTGTCTT TAATAGGATT TACTGCTTTC CATTCCTTTC CATTCCTTTC CATTCCTTTC CATTCCTTTT CATTCCTTTC CATTCCTTTT CATTCCTTT CATTCCTTTT CATTCCTTTT CATTCCTTTT CATTCCTTTT CATTCCTTTT CATTCCTTT CATTCCTTTT CATTCCTTT CATTCCTTTT CAT
52951 53001 53051 53151 53201 53251 53251 53301 53451 53451 53601 53651 53601 53651 53751 53801 53851 53901 53951 54051 54101 54151 54201 54251	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTT TATGTATATA GTTACATAGC AAGTGAGCAT TCCATCAGGC TCCCTTTCCT TTTTTTTTTA ACCTGTATAG CTCCATCCAT TTTTTTTTTT	ACAAACCACT TTTTTTAAG TCGGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TTCACCCATA TCACCATACTG TCTTCCTGGTGAAAA TTTGAAGAGT GTTACTGCAA TTTGATTCTT GTTCTTTTTT GGGGTGATCT CCCTGCCTCA TCCAGCTAAT CAGGATGGTC AAAGTGCTGG TTTCTTATTGA TATGCATTCT GTGAACAGTG TCGTGAACAGTG TCGTGAACAGTG TCTTTTTTT TCTTGAACAGTG TCCTGCCTCA TCAGGATGGTC AAAGTGCTGG TTTCTTATTAT ATGGTAGTTC GAACTAACTT CTCGCCAGCA	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCA TCCTCCAAAA CTTTACACAA TGACCTTCTG GGCTTTTTT CAACCTATAT AATTATTAAC AAGACATGAC TATTTTGGCC TGAGACAGCA CGGCTCACTG GCCTCCTGAG TTTTTTATTT TCAATCTCTT AATTACAGGC CTGTGTAGTA ATCATTGATG CTGCAGTGAA ATCATTGATG CTGCAGTGAA TCCTCTGGGT TTCTTTTAGC ACACTCATAC TCTGTTACTT	CTTIGGCTAT GCTTGAATCT CCTGCCTCAG CTGGTGGCAG CTTCTGACAG GCGAGAGAGG GCTGAATTCA AGTCTAGAAT AGATACTTT TTTCTTCTTC ACAGAATAGT AGTCTTATTA CTTATTCTTT CTTTTTCAGA TCTGGCTCTG CACCCTCTGC TAGCTGGGAC TTAGTAGAGA GACCTGGTGA ATGAGCACC TTCCATGGTA GGCATCTAGG CATTCACGTG ATTTCACGTG ATATGCTCAG TCTTTGAGGA ATTTCACGTA ATTTCACGTAC ATTTTCACGTA ATTTCACGTAC ATTTTCACGTAC ATTTTCACGTAC ATTTTCACGTAC ATTTTCACGTAC ATTTCACGTAC ATTTTCACGTAC ATTTCACGTAC ATTTCACCTAC ATTTCA	TIGGIGCTIT TGCIGAGGCT CCTTCCAAGT TGCTCGTTGA TITTIGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGIG CCCTCTCCAT TTCTTTTTT ACAAAAACATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT CTCCTGGGTT TACAGGCGGG CTGGGTTTCA TCTGCCTGCC ACGCCCAGCC TATATGTACC TTGATTCCAT CATGGGTTT TAATAGGATT TAATAGGATT TAATAGGATT TACTGCTTTC CATTCCTTTT AGGTGGGAGC
52951 53001 53051 53101 53151 53201 53251 53351 53401 53451 53501 53651 53601 53651 53751 53801 53851 53901 54051 5401 54051 54101 54251 54201 54251 54301	ATGTATATGT TTTTTTTCT GGATTCAAAC AGCTGGGACT ATGTTCTTTT TATGTATATA GITACATAGC TCCATCAGGC TCCCTTTCCT TTTTTTTTA ACCTGTATAG CTCCATCCAT TCATCAGC TCCCTTTCCT TTTTTTTTA ACCTGTATAG CTCCATCCAT TCAGAGGATTCT CAGAGGATCTT GGAGTTCAGT CAGAGGATTCAGT CAGAGGATTCT TGCCACCACA TCATGTTGGC TCGGCCCCCA GATCTTGTTC ACATTTTCTT GTCTGCTATT TGTGGTAGAC GCTGGATTGA CACAATGGTT TCTCTACAAC TAAATGATAA	ACAAACCACT TTTTTTAAG TCGGGGCTC ACAGGCCTGC TCCTTAGTTC AGAAGGACTT TCACCTCACA TCACATACTG TCTCCCTGCT CTGTGAAAAA TTTGAAGAGT GTTACTGCCAA TTCTTTTTT GGGGTGATCT CCCTGCCTCA TCCAGCTAAT CAGATGGTC AAAGTGCTCA TCCAGCTAAT CAGGATGGTC AAAGTGCTCG TTTCTTATTCA TATGCATTCT GTGAACAGTG TCGTTTAAT ATGGTAGTTC GAACTAACTT CTCGCCAGCA GAACTTATGA GAACTAACTT CTCGCCAGCA GAACTTATGA	TAGTCCTGTG ACAGGGTCTT AAGTGATCCT ACCACTGTGC CTTCCTAGCT GGTTGCCTCAAAA CTTTACACAA TGACCTTCTG GGCTTTTTT CAACCTATAT AATTATTAAC AAGACATGAC TATTTTGCC TGAGACACCA CGGCTCCTGAG CTTCTTT AATTACAGGC CTGTTAGTT AATTACAGGC CTGTTAGTA ATCATTGATG CTGCAGTGAA TCCTCTGAG TTTTTTTTT TCAATCTCTT AATTACAGGC CTGCTGAG TTTTTTATTT TCAATCTCTT AATTACAGGC CTGCTGAGT TTCTTTTACTT AATTACAGGC CTGTTAGTA ATCATTGATG CTGCAGTGAA TCCTCTGGGT TTCTTTTACTT ATGTAAAGAA	CTTIGGCCTAT GCTTGAATCT CCTGCCTCAG CTGGTGGCAG CTTCTGACAG GGGAGAGAGG GCTGAATTCA AGTCTAGAAT AGATACTTTT TTTCTTCTTC ACAGAATAGT AGTCTTATTA CTTATTTCTTT CTTTTTCAGA TCTTGGCTCTG CACCCTCTGC TAGCTGGGAC TTAGTAGAGA AGCTGGGAC TTAGTAGAGA AGCTGGTGA ATGAGCACC TTCCATGGTA GGCATCTAGG CATTCACGTG ATTTCAGTTA GCATTCAGTTA GCATTCAGTTA GCATTCAGTTA ATTTCTTAGAGA ATTTATTAGAGA AGTATTATTAT GGAAACAGAC	TIGGIGCTIT TGCIGAGGCT CCTTCCAAGT TGCTCGTTGA TITTIGGGGCT ATGCAGTAGA TAAGTAAACA ATTTATGGIG CCCTCTCCAT TTCTTTTTT ACAAAAACATG TTCTTCTTAA TCTAGACCTG TCACCAGGCT CTCCTGGGTT TACAGGCGCG CTGGGTTTCA TCTGCCTGCC ACGCCCACC CATATGTACC TTGATTCCAT CATGTGTCTT TAATAGGATT TACTGCTTTC CATTCCTTTC CATTCCTTTC CATTCCTTTC CATTCCTTTT CATTCCTTTC CATTCCTTTT CATTCCTTT CATTCCTTTT CATTCCTTTT CATTCCTTTT CATTCCTTTT CATTCCTTTT CATTCCTTT CATTCCTTTT CATTCCTTT CATTCCTTTT CAT





54401	TGGTTACTAA	GCTTAATACT	TGGACAATGT	AATAATATGT	ACAACAAACC
54451	CCTGTGACAC	ATGITTATCT	ATGTAACAAA	CCTTCACATG	TACCCCTAAA
5/15/01	CCTAATTTIT	TTTAAAAGAA	ACAGAATICCC	AGCCAGGCAT	AGAGGCTAAT
24201	TOOTETAAT	CCCAGCACTT	TICCONCICTIC	AGATGGGCAG	ATCACTTGAG
54601	CCCACCACTT	TAAGGCCAGC	CCACCCAACA	TAGCAGAACC	CCATCTCTTC
24021	AAAAAGIACA	AAAATTAGCT	CCACCATCCC	GIGIGOACCI	CACCTCAACC
54/01	CCCCTTGGGA	GACTGAGCTG	GGAGGATGGC	TIGAGCCCAG	GAGGICAAGG
54751	CTGCAGTGAG	CTGTGATCAT	GCCACIGCAC	ICCAGCCIGG	GCGACACAGC
		CTCCAAAAAA			
54851	CAACTGCACT	TCTTCACTCC	CCCACCACTC	TAATGAAGTC	ATCACTAACC
54901	CACTTCTAAA	GTACTCACAT	ACCCTATGTC	TATGGAGGTA	TGTCAGTGGA
54951	GGCTAAGGTA	TGCCAGTGGA	GGCTTATGTA	CCTTATGTCT	AAATATTTAA
55001	AGTTATTAAA	TTAAAAAACC	ATTAAAATAT	GCTTTCTACC	TTGACAAACC
55051	TTTATAACAA	AATTAGAAAA	TGTTTAATGT	TATGGCATTA	AATAATTGAA
55101	AGCAAAATAT	CAAAGATGAT	AGAATTTAAT	TAATTATTTT	ATTITATTITA
55151	ATTTGAGAGA	GGGTCTTTCT	GTGTCACCAA	GGCTGGAGTG	CAGTGATGCA
55201	ATCATGGTTC	ACTGCAACCT	CAACTTCCCG	GGCTCCAGTG	ATCCTCCCGC
55251	CTCAGCCTCC	CAAGTGGTTG	GGACTACAGA	CATGTGCCAC	CAAATCCAGC
55301	ΤΔΔΤΙΤΙΤΔΔ	ATTGTTTTA	ATAGAGGTAA	GGGTCTCACT	ATGITGCCTA
55351	CCCACTCTC	GAATTCCAGG	GGCTCAAGGG	ATCCTTTIGC	CHECCHIC
		GGATTTAAGT			
		ATATTTCACA			
22277	TOTALIA	AATAATAAAG	TAAATCAAAG	ACATATATTT	CAAAATTATC
		AAAAAATTAA			
		ATCAAGATAT			
		TAAAGATTAA			
2202T	AGIAATGATG	TTAAATTTAA	AATTCCAATAC	CACCTCCCTC	CCATCCCTCA
22/OT	COCCTCTAAT	CCCACCACTT	TECCACECCA	ACCCACCCCC	ATCACCTCCC
		CCCAGCACTT			
		CAAGACCAGC			
		AAATAAGTTG			
2220T	IACICGGAG	GCGGAGGCAG	GAGAATCACT	CCACCCAGGG	CAACAACCCC
		CGAGATCACA			
20001	AAAACICIGI	CTCAAAAACA	AAAAGAAACA	AAAAACACAG	COALANTACC
2002T	ATTAGCACCE	CTCAAAATGA	AATACTTAAAG	TATAMATCA	GCAVATAGG
		ATATAAGTAA			
2012T	GAACCAAATA	AATGGACAGA	IATICCAIGI	TATIGGALAG	GAAGACICAG
		ATGTCAGTCC			
		AATCCCCGCT			
		TGTGGACAGG			
		AAAGTTAAAG			
		TCAACTCATT			
		CTTCAAGACT			
		GAAAGAATAG			
		GACCCAGACA			
		TGGAGGAAAG			
		CACATGTAAA			
20\0T	TICACAAAAA	TGAACACAAA	AIGGAICAIC	AACCIAGACA	IGAAACACAA
					GAATGAGAAG
2000T	ACTIGGAAAA	TATTIGCAAA	AGACACATCT	GAIAAAIGAI	TCTTATCTAA
26821	AATATATAGG	AACICTIAAA	ACTGAACAAT	AAAAAAGAAA	CCTGATTTTA
		AACACTCTAA			
		CATATGCAAA			
					AATGGCCAAA
		CTGACAACAC			
					CCACTTTGGA
		CAGTTTCTTA			
57201	ACAATTGCAG	TCCTTGATAT	ITACCCAAAG	GAGTTGAAAA	CTTATATTCA
					ATAATTGCCA
		GCAACCAAGA			
		TCCAGAAATG			
		AAAAGACATG			
					CACAATTATG
57501	GCTCACTGTT	GCCTTGACCT	CCTGGGCTTG	AGCTCTCTTC	CTGCCTCAGC
		GCTGGGACTA			
57601	TTTTTTGA	GAGATTGGGT	ट्राद्धावा	TGCCCAGGCT	GGTTTTGAAC
57651	TOCTGGGCTC	AAGTGATCTT	CCTGCCTCAG	CCTCCCGAAG	TGCTGGGATT
					тттстст
57751	AGAGACAAGG	сспсстт	TATTGCCCAG	GCTGGAGTGT	AGTGATGCAG













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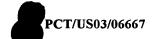






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The temperature of the second





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75001	TAAAAAGAAG	GAGGATATGC	TGACAATTTG	AAGTGTAAGG	ATGGGTGGAG
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	ACAAAGAAAC				
	AGGATTTGCA				
	CATCACCCAT				
	AAACAACTAA				
	AACATAATTT				
	ATAGGACTGA				
	TTATTTGCAT				
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	TTTAAAGCTG				
	GGGTAAATTC				
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	TATTGGTTCT				
	CAGTCAAAGC				
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	GAACATTTCA TCACAATCTC				
	GTCCCATAGC				
	ATTGTCTGTG				
	ATTGACAAAG				
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	GCTGGAGTG				
77601	GGTTCACACC	ATTCTCCTGC	CTCAGCCTCC	CAAGTAGCTG	GGACTACAGG
	CGCCCGCCAC				
	TTTCACCGTT				
77751	CCGCCTCGGC	CTCCCAAAGT	GCTGGGATTA	CAGGCGTGAG	CCACCGCGCCC
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	GAATTTTAGA				
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77951	AACTAAACAT	GICAGITAAT	CCTGTTTACC	TCTCTTTIGG	ATGCTCCAGG
78001	AGCCCTCTGT	AGTATTCAAA	AGTAAGGGGT	CAGAAAAGAC	AACCTTGAAA
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	CTTTATATTA				
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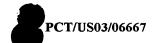
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			ATACCCTTTT		
			AGATTAATTT		
			TTAAAACAAT		
			GCCTTCTTAT		
			TGATGTAAAT		
			CTTAGCAATT		
78701	TGGTAAGTTA	TTTTAATTAT	GTGCTACCAA	TTATACCTTA	AGTTGTAGCG
78751	ACTCTGGTGT	GCTATTGGTA	ATATGGCCTT	ACAAAACTGA	AAAGCAAGCA
			CCCAAGAAGC		
			TGGGAGACCC		
			CTGGCTAACA		
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			CACTGCACTC		
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79251	TITATTITC	AAATATTAAA	ATCATTTGAA	CTAAAAGGTA	TTATAGCTTT
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			ACCTCAGGAT		
			TAGGGCCTAA		
			GGATTTATCT		
			TTTTCTAAAA		
			CAGGCCATCA		
			CAAGACAAAA		
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			AATCTTTAAA		
			AGTTGTTCAT		
			TATTAGCCAG		
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			GTCAAGCTCC		
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			GGCTTGAACA		
80401	GICIGIGIIC	TATOCTGTCT	TACTCCTTAT	GACAGAACTG	TACAGAAAGA
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			CTTTACAGAA		
			ACAGGGAGAA		
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			GCAGTTTAAG		
			GTTTAAATAG		
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			GACCAATATT		
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81651	ACCTITIGGAG	CAAAAAGTGG	GCATTTTTAT	AAGGTAGGGG	AGGAAATGAG
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81751	CTTGGGCAGA	AGTAAGTTGT	AAAAGTGGCC	AAGTGGGTAT	GCTTTCAACA
81801	TGCCCTCCTA	GTGGGCATGA	GTTCTGAGAT	GACCCTGTGG	AGAGTTCTGT
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81901	CTTGGGGGGA	AAATATATAT	TAGGAAGTCC	TCTGTGGGTG	TTTTGTAGAA
81051	GGACCTAGAG	GGACTAGGGC	TIGATIGITA	TTATTTATT	TATTTATTTA
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8/62T	CATTIATICC	AACCCAGGIA	GAGAATTOCT	GICIGIICII	IAAAAAAAAGA
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88251	WANTED TO THE PERSON OF THE PE	CACCATCCAT	GGAAAAATTC	TTCTCAAAC	TIGHT TO THE
88301	TECCAMAME	ATTROCCATT	CTGTATTAG	AAGAAAAGAC	ACAGTGCACT
88351	CAACACCCA	TCACTGTAAG	GAACTGGATTCG	GCACATAACT	GCATGGAACA
TCCOO		,			







88401 TCTCTCCCTG CAGCTCTAGT TCTCCTTGTA AGTCCCTTGC GTTGGTAGAA 88451 TAATCCTCAG TTAGACAAAC ACTGATTTAA TATGTAGCTC TGGCTAACAG 88501 GAGGTGATTA AGAAGAAAAC CTCTTAAGAT GATTTCCATC CTTTGTCTCT 88551 ACTITAGTGG TITTATCTTCA TITTCCTGCCT CTTTCCTGTC CCTAGCTGTC 88601 TTTATGCTGC TTTAGTTGAA AAGCGTTAAT GTGGTCATTA AGGAAAAATA 88651 AGTCAAATTT ACATTIGACT TITTATTTTT AAATATTTAA TCAACAGAAT 88701 CCTTGGTTTT ACTCATTGCC GCCCCCCACC CCCCAACACA CATCCCTTCC 88751 TCAACTCTAA AGTGAGCCTC ATTCTTTCAT ATTTTCTTCC ATCTAATTTA 88801 GAAATTCTAT TTGGATTTTT AAAAATTATA TTTATTTCTT TGTAGAAAAT 88851 AGATATTITIC ATCITTANAG TACCTITATIG GGITTITICT TCTANAATIG 88901 TTTTTTANAG ANAMAGITT TATTTIGGAAT AAGATTCTIG TAGGTAATIC 88951 CATGAGATGA TITATTTTAG CAGCAACATA ATATTTACAT TATTATTAAT 89001 GTAATTAATG TTATTAATAC CTCATCAGAT AGCTTCTTTG ATCTGGAAGC 89051 TTCCAGGTAC CTATTGTCAG TACTTGTGGC TCTACCACTT GCCGAATGTA
89101 TTACAACTCT AGTTGTGGTA GAGAGGGGAC TGAGAGGTAG ACAACTTATG 89151 TAATCTACTA CCTAGTTTGT TAACAAAACA CACATACAAA GCAATGTTTT 89201 TCAAATTTTT CTGACCACTG AGCAATAAAA ATTATGACAT ATATTTTGAT 89251 GTGACCCAGT TCTGTCTCTC TTTCTCTACC CTCTAAGTGA AACAAAATTT 89301 ATTGAAACCA AAATTCCCTT ACTACATGTA ATATTCTCAT ATATTCTATT 89351 AAATTTOGTT ATTTAGCTTG CTGATCAAAG GCTACTGAAA CTTGAGAGCA 89401 AGATACAGGA GCAAGGGGAA ATGTGGTATA GATTCTGAGT GTCAAGTGGC 89451 AGGTCCATTT TTTCCTCTAG CTCCAGTTCT GCCTTCTGAG GAAAACCTTC 89501 TCCAACAACT TAGGTCAATC ACACCCATGT CCCTTCTCTG AATCCTTTTT 89551 GCACATATGA TTGGTATCCG ACAGCCTTAC TCATTTACAT TGCACTTATT 89601 TGGCTGCCAA ACGTCACAAA CTGGAACCAT GTGTTACTGA AGGGAAAACC 89651 TGGAAGTGAA AAGGGTTCAG CAGTAGTGCA AATACCATCA TAAAGCTCAT 89701 ATACTICACT CTGCAGGAGG GAGAAGCTCT GTGGTTTTCC AACTGAGAGC 89751 ATTACAGTAC AGTGATACCA CTGTACAGGA ACTGATGTTC CTGATGATTC 89801 TGCTGTGAAC AGTATTTTTA ATATACACTT TGAAGAAGGC AGAGAGAAAT 89851 GTATAATAGA CITAAATTIT TITICTITAAA ATTIGITAAAT AAAAACAAAT 89901 AAGCACTITA AGTAAGITAC AATTATCTGG AAAACTACTT AGGTGGAAAA 89951 ACTGATACAG AATGAATGAA GTATTAATTT CTGTTTTGTT CTGTGTTATT 90001 ATTATTTGGG ATAGATGTCT TGTTTCTTTA AGCAGACTAT GAATATCTTG 90051 AAGGCAGAAC CACATTTTT TTTTTTTTGA GACAGGGTCT CACTATTACT 90101 CAGGCCAGAA TGCAGTGGTG TTATCATAGC TGACTGCAGC CTGGATTCCT 90151 GGGTTCAAGC CGTCCTCCTG CCCCAGCTTC CTGAGTAGCT AGGACTACAG 90201 GCATGTGCCA TCACACCCAG CTAATTTCAG CTATTTTTT TTTTTTAAA 90251 TAGAGATIGGG GTTTTIGCTAT GTTGCCAGAC TGGTCTCAAG CCATCCTCCT 90301 GCCTTGGCCA CCCAAAGTGT TGGGATTACA GGTGTGAGCC ACCACGTCTG 90351 GCCAAGGACC AGATTTTTAA TATTCTTTTC CACAATGTAT CTGGTACACA 90401 GTAGTTGCTT AATATGTTGG CTAAACAAAG AGTGGAGATT CAGTAAAGGG 90451 TGATCAGAGT GAGGTGAGAT TAATTTGGGA AAGCCTAGAA GTGATTCTTG 90501 AGCCTGATTT GAAGGTGGTG CTAGCTGTGG ATTAATAGAG GGAGAAGGGC 90551 ATCTCAGAGA GAGGATTGCC AACATGCCTT AATTTTATCA GATTCTAGAG 90601 TTCCTTATGA TTACCTCAGC ATGTTGCTAG ACTAGCATTA TTATCCAAAA 90651 TTTTAATTAT TAACCAACTT TAATCITACT TTCTAACAAA TTGTTTGCTT 90701 TTACTACTGA TAGCCTTTTC AAAAAACTTT AACTAGTTTT ATTCCTTACC 90751 ATAATTGTTT CAAAGAACAT AATGATATGA TCCTTTATCT TCCTAAGAAA 90801 TGTGCAATTA TTTGGTTAAA CTGTAAGATT ATTTAATCCA TTATTCTTTT 90851 GACACATGCA TGGCCTTACA GCTTACAAAC TGGGATCACT AAAGGAATAC 90901 ACITAATITA AGICITICIG TAGICAGAAT ATGATTICIT GITGICITGC 90951 ACAATACIGA GAACAGIGCA GTACAGGGCG AAGGITGGIC TACAGCCCTT 91001 AGGCCAGCAA AAACAGGCAC AACTGCACCT CTGTGCAAAT GTTCCTGACA 91101 TIGGTAAGTA CCTGGAAAAA CTCCATGAAA TAATTAGATT TCATAGTTAA 91151 TICTAACTTT TTTAAAAAAT GTTTCATTGA GACTAGGTTT TTGGTTTGTT 91201 AATTGAATCA CTGTTGATTT TACCCCTTCCT GGCACCAACC TTTATTTCTG 91251 AGCTGTGGAG AGCACAGTTC TCACTCAGTG CTGTGTGCGT CACCTGAAAT 91301 CCACAGAAAG AGGTGGCTGA ACAAAATCAC TGATGACCTT AATGGTTATT 91351 TITICACATAT TCAGATTAAA TTAAAATACG TTTAGTGCTA CATGCTTGAC 91401 TTACTGAGTT TTTCCCTCTA TTTTGGTTAA TTTTTTTTT TTTTGGTTAA 91451 CITITACITG TAGAAAATAT GITGATGAAC AAAAACCCAC TTATACTATA 91501 AGATTTTATT CTACCAAGCA CACAGTAACA ATATTGAAAG CTGCTTTCCA 91551 TCTTTTTCAT CTTTATACAG TTCCATCGAG CCTCTGTACC TTACCTATGG 91601 AATCATATTT GCCTGCGGCT GCTCCTTTGC ATACCAGCCT TCATTGGTCA 91651 TTTTGGGACA CTATTTCAAG AAGCGCCTTG GACTGGTGAA TGGCATTGTC 91701 ACTOCTOGICA GCAGTIGTICTT CACAATICCTG CTGCCTTTGC TICTTAAGGGT 91751 TCTGATTGAC AGOGTGGGCC TCTTTTACAC ATTGAGGGTG CTCTGCATCT





91801 TCATGTTTGT TCTCTTTCTG GCTGGCTTTA CTTACCGACC TCTTGCTACC 91851 AGTACCAAAG ATAAAGAGAG TGGAGGTAGC GGATCCTCCC TCTTTTCCAG 91901 GAAAAAGTTC AGTOCTOCAA AAAAAATTTT CAATTTTGCC ATCTTCAAGG 91951 TGACAGCTTA TGCAGTGTGG GCAGTTGGAA TACCACTTGC ACTTTTTGGA 92001 TACTITIGIGO CITATGITICA CITIGGIGAGI ATGCTOCTIC ACTGATCATG 92051 AATATTACTA TITTAATAAAG AAAAACTTCT TTGAAGAGAA AGTTAGGTCG 92101 AGTTAAAGTT GGCCTCAAAC ATTATCCTGG TTGTAATTTT GGTATTCTTG 92151 AAATGAAAGG TCTCTCAAGA CAATGTCAGC ACATCCATTA GACCACTAAA 92201 CAGAGAGAGT ATGTTTCATA GTGTGCTTTG GTATTTTAAA AACCCTGCAA 92251 ACCCAGCCAG ACACCATGGT GCCTGTCTAT GGTCCCAGCT ACTAAGCTGA 92301 GGCAGGAGGA TCACTTGAGC CCAGGAGTTC GAATCCAGCC TAGACAACAT 92351 AGAGAGACTC TACCTCTAAA AATAAAATAA ATGTCCCCAA ACAAACACAA 92401 TGTTTTTAA CAGGAAGGCT AAAATAGTGG AACAAATTAC AATCAGTATA 92451 AAACATTTGA TAGGTCTCTT TITCTTCATA TGGCTTTTAT CAGGGACAAA 92501 GCTAGOGCTA TGATTITGCT ACCATAAGTA AATTGTTTTT CAACCGAAGG 92551 GTGTAGGTAA TTAGCAAAAA AGCCATGATG TTGATACAAA GAAACATTAC 92601 ATCTACTTGT GGTACACTTC TGGGAAAATG GGAATTCTAT TCAGAGGAAT 92651 ATCTGAGAAA AGTTACTCAA GATCTAAATG AGGAAAGAGA ACTATGGTTT 92701 TATAGGAAAT TAGGATTTCA AGTGCTCAAG AAGTTTATAT TGTTTATTTC 92751 TATTTCAAAG GCAAAATTCA GCTTTGTTAT ACTGAAATAC GAATAATTAA 92801 TGTCTAGACT GGGGTTGGTG CCTCACGCCT GTAATCCCAC CACTTTGGGG 92851 GGCTGATIGCA GGAGTTCAAG ACCAGGGTGG GCAACATAAG GAGACTTCAT 92901 COCTACCTGG GGAAGGAAAA AAAAAAAAGA AGGAAGAAGC AGTGTCTAAA 92951 GTATCTGCCC CTGGCAACGT TTGTTCAAAA GTGTTCATTA TGTTTCTTCC 93001 TTTTTTCTTT TGTGGCTGAA AATGTATTTA CAATTCACCG TAAATGATAA 93051 AAATGGCATT GGCACACATA TITGTATGTT TGTGAACTTG GATTTTTTTC 93101 TAGCTTACAG TCTACTTTTG GAGATTTGTG CAATTTTTCT TTAGTTAAGA 93151 AATAAGTATA AATATAACCG ATTTACGGAC TATCAGGCTA CATCCTGATC 93201 TGATAGTCCA TTTTCATACT ATTAGGAAAG TATAGCCGAA CCAACTTAAG 93251 GTAAGTTTCC TGGAATATAG ATCTGTTGTG ACAGGATTAA CTTTACCATC 93301 CAACCTCTTT CATAGCTTCT GTAGTCAAGA GAACATTTAT TGTGTCCTTT 93351 CITAAAAAGA TGAGTAGAAA TTCTTTTTCT TTTTTTCTT TTTTCCAGAC 93401 AGGGTCTTGT TAAGTTGCTC AGGCTGGCTT CAAGCAACCC TCCTGCCTCA 93451 GCTAGGATTA CAGGTGCAAG CCACCACACC CAGCTTTAAA AAAAAAATTC 93501 TCTTTGGTAC TACCACATGA ACACACCTAG AGAAATCATA ACTCAGCTTT 93551 GCTAATACTA GACATTTACC AAAGGAAAAG TGGTAGATGA CTGTCTAGTT 93601 ATTITIGGTT ATATATTTAT AATTIGTAAA TTAATTICAC ATATATTACT 93651 TCATTTGACT TTCACAATAA ACCAGTAAAG CAGATAAAAT AAATATTAGC 93701 TCCAATTTTA CAGACTGAAA AACAGATCTA TTGTTAATAG AGACGTTAAG 93801 TCTTCCACTG TGCTTACCTG GTAGCAAAAT CAGTCTACAG TCTTAATAGC 93851 ATATTIGGGCC ACTTICCCTIGG ATATATTACC AAATGTGTCC ATCTTATTAG 93901 GGGAAAAATG AGTATGCCTA AGGAAATTTA ATAAGCATGT TATTTCTTCA 93951 GGTAAATAAA ATTTCATAGT GGAAGGTGAG TTAGACAATG TTATAGATAC 94001 TTTTGTGATC AGGAGATGGC AAATCAGATG GTGCACAGAA CAATAAAGTC 94051 TCTGTTAATT CTGTTAATAA ACCATGCCTT TTTTCTGCTT TCCCTTCTTC 94101 CAGGCATGTT TTCTTACAAA ATATGTTGAC ATTGTTCATT TGAGATTTTC 94151 TCTTTCTCAT AACGGTGCCC GTTATCGCAC CGAATGCAGC ACGGTAGAGG 94201 AAAGATCAGA TAGCTAAATG CCATACAGGT GTTTAAATCT CCTCTTTGGT 94251 TATGTACTGA GTTTGTCACT TTGTTGTAAT TTAAGGTTTG AATTATGGAT 94301 ACTTAACCAG GAATGGGACA CTAGTTTCCT CCTTATACAG GGAAAAGGTG 94351 TCTCATATCC TTCAAAAGAC TAGTAAAGTA GATGATGTTC AATTCCTACT 94401 AAACCCTTTA TTGACTGTTG AGGGGACACA TATATGAGAC GTAAAAATTT 94451 GCTCTGAAGG AGCATAAACC TAGTACATGT AATTAAAAAT GGCTACAGTT 94501 TATAAAGCAC TTTTACATAC ATTCTCTTAT TTAATATTCA CAACAATGCA 94551 GTACCTGTGG TGTATCCTCT TTATTTCATG GAAGGGAAGA CTAAGGCCCG 94601 GAAAGATTAA ATAACTTGCT CAGCCAGGCA CAGTGGCTCA CGCCTATAAT 94651 CTCACCACTT TGGGAGAATG AAGTGGAAGG ATCACTTGAG CCCAGCAGTT 94701 CAAGACCAGC TIGAGCAACA TAGTGAGATT CCATCTCTAC AAAAAGTAAT 94751 TTAAAAAAAAT TATCTGGGCA TGGTGGTGCA TGCCTGTGGT CCCAGCTACT 94801 TGGGAGGCTG GGGTGGAAGG ATCGCATGAG CCCAGGAGGT CAAGGCTGCA 94851 GTGAGCCATG ATGGTGCGAC TGCACTCCAG CCTGGGTGAC TGAGTAAGAC 94901 CCTATCTCTA AAAAAAATTA TAAAGTATTC TAAAGGAAGA ACAGATTGAA 94951 CAATTTTTAA TTTATTTGTC TCCTCCTCCT AGTGGCAGCC TTTTAAATAT 95001 GGAAGGTGAA GAAATAAAGA GCCAGATGTG GTGGTACACA TCTGTAGTCC 95051 TAACTACTCA GGAGGCTGAG GCAGGAGGAT TGCTGGAGCC CAGGAGTTCA 95101 AGGCTGTGGT GTGCTATGAT TGTGCCACTG CACGCCAGCC TGGGTAACAG 95151 AGCAAGACTC TGTCTCTAAA AAACAGATAA TAAATAAAGA AGTAACTTGC





95201 TTGAGGTCAC AGAGATAGTG ACTGATAATT ATTACTGTAG TACTTTTATG 95251 TAAGAGGCAG TATTGTATAG TGGTTTAAAA GTGAAGGTTC TGGGCCTGGT 95301 GCGGTGGCTC ACCCCTGTAA TCCCAGCACT TTGGGAGGCC AAGGCAGGTG 95351 TATCACCAGA GGTCAGGAAT TTGTGACCAG CCTGGCCAAC ATGGTGAAAC 95401 CCTGTCTCTA CTAAAAGTAC AAAAATTAGC TGGACGTGAT TGCTTGCACC 95451 TGTAATCTCA GCTACTCAGG AGGCTGAGGC AGGAGAATCG CTTGAACTTG 95501 GGAGGCAGAG GTTGCAGTGA GCTGAGACCG CGCCATTGCA CTCCAGCCTG 95601 AAGTAAGACA GATCTGGATT TAAATTCAGG TTTTGTTTCT TACTAGTTGC 95651 ATAACCTTGG GCATCCTCTG TAAGCATCAG TTTCCTCATC TATGGAGATA 95701 AACCCAATTT TGCAGAGTTG TGAGGATTAG ATAAAATGTA TGTGAAACAT 95751 CTACCTCAGT TCTGGCATAA AAATGGGAGT TATTTTAATG TAAGGCAATG 95801 TGATTGCCAA CTTGAGATAG AAGTAAATTT TGAAAGGAGA AAGATAATAC 95851 CCATTTGGAA AAGTGGTTTT AAAAAGTTTC ATAGCATTGG AGTTGGGCCT 95901 TGAGCATGAG ATTITIGIGTA CAAATCIGAT CITTGATCAA CTAGGGAACT 95951 AACTTACCAG TITAGGICIT TGAAGATTCA GAAATACAAT GGAGTGCTCT 96001 CATTGCTATG TTAAAAATTC TAAGATCTTA TTAGATTGTA CATGATGATT 96051 TGAGAGAGAA TATGTATGCT TGCTTTCAAA GTGAGGTTGG AGGTTTGATC 96101 TICTCGTAGT TGACGTTTCA AAAAGAAGAA TTAGATTGCC TCCTCGAAGC 96151 TAAATTTACC TTTCTTTTAG GCCTTCCCAC TTAAAATCTT TTTTAGAAGG 96201 ATACAAATCT TATAGATCAA TTTAGATGAG GCCTAACTTT CTAAAAACGA 96251 TICCTAGTAG CAGCIGCATC AGITTITATG AATTIGCCCCT TITTGCCTGAG 96301 AGTIGTTTTG TITTIGTTTTC TIGGAATCTTT TITTIGTTTTG TITTIGTTTTG 96351 CTTTGTTTTT GTTTTCGTTT TTTTTTGAGA CGGAGTCTTG CTCTGTCTCC 96401 CAGGCTGGAG TGCAGTGGTG CAATCCCGGC TCACTGCAAC CTCTACTTCC 96451 OGGATTCAAG TGATTCTCCT GCCTCAACCT CCCTAGTAGC TGGGATTACA 96501 GGCGCCTGCC ACCACACCTG ACTTAATTTT TTGTATTTTT AGTAGAGACA 96701 AACGGCTCCT CTGACTCCTC TCATTTAGCT TTCAGGAGCA TAAACTCTCT 96751. TGGTTTTCTG CCTACCTCCA CATCACTCCT CCTTAGTTTC TTTGCTCACT 96801 TCTTCTTTT CCCACTGACC CCTGAATATC AGCATGTCCT AGGGCTTGTC 96851 CCCTGATCTT TTTCTCCATG TATTCTACTG GTGGTTTCAT CCAGTCTCCT 96901 AAGTTCATAC ATCACGTATA TGTCAATGAC TTCAAATTTA TAATTCTGGT 96951 CCAGACCTTT TCCCTGAATC CTCCACCAGA GCTGTATATC CAGCTGCTTA 97001 CTTAACATCT CCACTTGGGT AACTGCTAGG TGTTTCAGAC TTACCCTGTC 97051 TAACCCTGAG GTCTTGATCT TACCCCTTAA AACTTACTCT GCCCCCAGCC 97101 ATCCTCATCT CAGGAGCTGG CAATTCCGCC CTTTCAGTTG ATCAGACTCA 97151 AAACTTTGGA GTCATCCTTG GCTCTTCTTT CTTGCACACC ATAGTCCTGA 97201 TCCAGTGAAG AAATCCTGGT GGCTTTTCTT TCAAAATATA TCCAGGATCT 97251 GACCACCTCT CACCATCCTC ACTACTCATA CCTTAGCCCA GGCTACCACG 97301 TACCCCTAGC CTGGATCACT GCCAGAGCCT CCTAACTGGT CTCTCTGTTC 97351 CTTCTCTGCC CCGCGGAGTT TGTTCTCTAT GAAGAAGCCA CAGGCATTCT 97401 TTCTAAACAT AAGTCACTCT GCTCAGAATC CTTCAATGGC TTCCCATTTC 97451 CCTAAGAGTA AAAACCAATA TCCTTACAGT GACCTACAAG GTCCTTCACA 97501 ATCTGGCCCC CACTACCTCT CCGAGCTTCC ATCGCTGTCC CTTGCCCACT 97551 CTGCTTCTGC CATTCGCCTT TTAATGGGGC TCACTCTGAC TACCTGCTTG 97601 AAACTTCCTG CGTCCCTTTT CCCCTGAGTA TTCACAAACC GCTCCTAGTA 97651 CTCCTTTICT TTTTTIGTAG CACTTAATAC TTTCTAACAT TATCTATTTT 97701 ACTTCTTTAT TGTAGTCATT GCTTACTATC QGTATATTTA CACGTCTGCT 97751 AGAATGTAAA CACCACAAGG GTAAGGATCT ATTTCATTCA GTGGTAGATC 97801 CCAAGCATICT AGCACAGTIGC CTAGCACACA CTGGGTIGCTIC AAATATTTIGT 97851 TGAATGACTA AATATATTCT GGGTGAGTCT GAAGTGACAC TGTATAAGTA 97901 ATGITICATTI TITICATCATT TGGATCTITA AAATTCICTA CITTGATGCT 97951 ATAATGATTI TICACATTCT GTACTTGCAG GACATGGTGT TATTAATATT 98001 TATTCAATAC TTATTCAACA AATAAGCTCA AACTAAGGAA ACCTCGGAAT 98051 AATTGAGTAA CCAGTAATGC TGTCCGTTGA TGGAGGAGAG AGTTGGTGTG 98101 TTTTGCTCTG ATTCACTTAT GCCTTTGCTG AAATTTTAAG ATAAATAGAA 98151 GAAATTTCTG GTCCCTCAAG TAACTGTGTC TTCAGTACCC ACTGAAAAAT 98201 CTCAAAGAGT CTGGAGTGGT GTGTTTAAGA ATAGGATGCA GGATGCAGAA 98251 ccataaccag gcctcaggtc tgcatagctt tggtcgagca ttgagcatag 98301 ggcctogtga gataactgat aaatgccaaa tatgacaatg ataaatgcca 98351 AATATGACAA TGATAAATGC CGAAGAATGA CAGTGACAAT GATAATGAAG 98401 TTACCAAAAA TGATGGTAAC TTTTCTCATT GGCATGAAAT GCTCTATCTC 98451 CAATCTGAAG CTGATGATGT AGTTTCAGTT ACTCTCATCT CTCTCCCCTG 98501 CTACTCAGAT TGAAAATCAG CTACTTAGTA CCTGTGTTCT TTGACTCTAG 98551 ACCATATCAT TGGGTCAAAT TTCAGTTTTT AAATTTTAGA TCCACATGGT







98601 TCTCTGTCAA GAAGATGACT GACTCATATT GAAATCTGTA AAATATGTAT 98651 TCATTAGCCT GTTTTTTAAA AACTCCCTTA TAAGTGGGTT GACTTTGTGG 98701 CAGATAGTAA TTGACTGTTC TCAAAAGAAA CTTTGACCTG GTAGGAAGAT 98751 CCCATTTACC TGATGCTATG GTTCAAGACA GACAGATCAT TTGCTTGCTA
98801 GCAGGGCAAT TAGGTGAACT TCAAGTCAC TAGTAATTGG AAATGATTTT
98851 TTTTTTTTT TGAGACTGAG TCTCATTCTG TCGCCCAGGC TGGAGTGCAG
98901 CGGCATGCTC TCGGCTCACT GCAACCTTCA CCTCCTGGGT TCAAGCGATT 98951 CTTCTGCCTC AGCCTCCCGA GTAGCTGGGA TTACAGGTAC CTGCCACCAC 99001 GCCTGACTAA TTTTTGTATT TTTGGTAGAG ATGGGTTTCA CCATGTTGGC 99051 CAGGTTGGTC TCAAACTCCT GACCTCAGGT GATCTGTCTG CCTCGGCCTC 99101 CCAAAGTGCT GGGTTATAGG CATTAACCAC CGCCCCTGGC CATGAATTGT 99151 ATTTTTAMAC CAGMATGMA AATTTGAGAC TAATAAGTCA GTACAGGGAG 99201 CATGTAMACC TOGAMAGGTA TTTTTTAGCT TTGAGTAGTG CCAGATGCTG 99251 CCAAGGGTCA ATCAACACTG GAATGTAGCT ATTAGACCTT GCTAGGCAGA 99301 GCACCTCCAT TTACACTGTG GTCAGAGCAG CAGTACTGCT CCAAGCCAGA 99351 GCTAAGGGCG CTGAGCCACG CAAATAGGAA CAGCATACAA GCCTTCATCT 99401 CTCTGTGGCT TCCTCAGAGG GAGATTCATG TAACATTTGC CAAGAATTGA 99451 TTATIGITCA AGCACTTCCC CAAAATCTCA CAGAACCACC ACAAGGATGA
99501 GTGTAATAAA TAACACATAC TTAGAGCCAA GGAAACAATT CTGCAAAGCT
99551 GTGCTTGTTC AAAGCCATTC GCATTATGCT TAAAGCTGGG ATTTGAACAC 99601 AGGTTTCAGA CAAATATGTC TGAAATATAC TCTTTTTATG AAGGAGTCTG 99651 CATTCCTTCA TTGCTAATCC AGAGATAGGA GTGCTGCTAT TTTCAGCCAT 99701 ACTGGGCCTA CACCAAAGAT TGCTTTGCAC GTTTCCCTTC TGTTCTCTCA
99751 GAACGAAGAA CAGAGGCCAT GTTGAGCTGT TCCAGCGCTC AGAGCATGCT 99801 TCACAGCCAG GGAGAAAACT CTGGAGGAAA CCAGCTTTTG TTTTGATATA 99851 ATTAATGGGA ATGAGAAAAT ATCTATACCC TTATTTTCAG CCCCAACTTC 99901 TCTTTTGATC TCAAGTACAT TGTGAATATG AGAAAACTGA GGCCATGCAG 99951 TTACTTTTCA CAACCTGTGA CAAGCAGAAC ATGGACCATA CATAGCTTTG 100001 TGTTCAATTT TGCTTTCTAC AGTAAACATT AAGCATAACA GAAGAACAAA 100051 AATGGACATG TACAAATTTA TAGCAAGATC TATCCTTTAT TTGATTAACA 100101 TAAATACTAT TGCAGGAAAA TGGAAAAAGG TAAACTGCTT GAAATTTAGT 100151 CACATATAAA CSCTCCGAGG CCACTGGTGG ATCATTAGTC TCCTGAGAGA 100201 GCTCTAAAGA ATTAGTGTGT TGGAAAACTG TTCCCTCCTG TTAATGTGTA 100251 AATTTCACCA GTGGGTTTTT TTTTTTTTA AGACAGGGTC TCACTCTCTT 100301 GTCCAGGCTG GTATGCAGGG GTGCAATCAC ACCTCACTGT AGCTTCGACC 100351 TCCCGGACTC AAGCAATCCT CCCACCTCAG CCTCCCAAGT AGCTAGGACC 100401 ACAGGTGCAC ACCACCACAC ATGGCTAATT TTTAATTTTT TGTAGAGATG 100451 GGGTTCTCAC CACATTGCCC AGGCTGGTCT CAAACTTCTG TGCTCAAACA 100601 AGGTTTTATT TGATAAAATG CAGTATACTT TGAATCATCT CAAATTTCAT 100651 TTCTAATATG GACATTGGCA TGTCTCAAAT CCTTGGACTA ATAATCAAAT 100701 TAAAGTTTGT TCAAGTTTGA GGAACCTAAA TTAGCCAATT AGATAAGGGT 100751 CCTTTCATGT TTTTATATCA ACTAGAAAAT AAATTGTTTT GATATGGGAT 100801 GAATAGAAAT AGAAATCTTA ATTTGAAGAA TCTTCCCCTT GTGAGGCTAT 100851 ACTAAATIGGC TTTTIGCCTGA TATTTACAAG GTGGCTTTGG GTTGTGGAGA 100901 GAGTTGTCTG ATCCATTGAG AGTACATTTC TTACCTTCAA CATCTAGGGC 100951 ATCCTTTGGG AGAAGCCCTT GTAGTCACTA ACTCTAAGGA TCATAGAGCA 101001 TAAGGGTAAG CAGGCCTTCT TATGTATTCA TGCTATCAGG AAGGGTCTTT 101051 AGCACCCAAA CAAAGTTCTA GGGGCTGTAC ATTGCTGATG TGTTAACCCT 101101 CAGCTGCCCA TGTAGCATCT ATTTACCCCT ATGCTTTCCC CACTTTCTAT 101151 CCCTATCATT ATATCTCTGG CTCTTTTGCC CCTCTCTCCT TGGGCAGCTT 101201 ACTIGIAATT AGAAAGITTA TATTCCCTCA TAACATATIG TAAAAGIGCT 101251 CATTTAAAGG GCAATGCACA CCAAATTGGA GGTGTATAAT TGCAAACATG 101301 GAATCCCTAT ATCTCTGTTA TGCAATCCCT GTATCTCTGT ATCCATGTTA 101351 AATTGAACTG ATGCTTTTTT GAAGTAAAAT GGTAAGAACA GTGGCAACAT 101401 CTAGTCTTCA GAGCATAGTT TAAGATTTTT GCCCAATCCT CCAACCCATG 101451 CAATGGTGTG CTTTGAAAAC CACAGGTTTC TTTTAGACAA ATACAACATT 101501 TATTTCCGC ATTTCTTTTT GATTTAACAT TTTAGTTAAC ATTTTTATTA 101551 ACATTTTAGT CTACAAGATG CTTCCACATT ATCTCTCATT GGAGTCTCAG 101601 GACCACTGTG TGAAATGGGC AATATCAGGG CTTCTATCTA GCAAGAAAAG 101651 AACCAGATTT GGGGTGGCGA AACACTTGC TCAGGGTTGC AAGGATGGTA 101701 CATOGTIGCAG CCAGGGCTTG AGCTTGGGTC TTCTTAAAAG TGTGGCTTTT
101751 AAATAAAATA CTTAAGTGCC TGCCAAAAAA GTATAACATT AACTTAGGAC
101801 CTGAAAGGCA TTGTACAGAT CAGGTAGTTG CACTCCTCCC CCTGCCCTAC 101851 AAAAAAAGAA AGGTAAAGGA ACGAAGGCAT GGAATAGTTA AGTTGCTTGC 101901 CAAAAGCCAC AGTTATAAAA GTAGCAGAAC TGGGTGTAAT ACCCAAGAAC 101951 ATCCATGGAA AATAAATGGA AGCTTATTAC AGCCCAGCCT GTAAATATGT





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102001	ACATAGAAAC	AGAATGTGTA	TGTAGAAACA	AAATTATTAG	AGGAGTGAAA
	TTAGTTTCTG				
	GGAGGTTGCT				
102151	AGCAATTGCA	ACTGGCTTTG	пысттст	TTCATGGATC	TATTTGGAGC
102201	TCAGGGACAA	GGTTGTTATG	CCGCAGATTG	TCCCTGACAA	TGCAAGGCTC
	ACAGTAGTAT				
102301	GGCTGCTGAA	GGTGACCTCT	CCTTCATGTT	GGTTGGTTTA	TCTTTGTTGG
102351	गाउदागदादा	TTATCTCTGT	TCACTATAAG	GTTCTGACAG	AAGCAAAGTC
	TTGGTCCCCG				
	TGGAAACTTT				
102501	CCTATCTCAG	TCAGCACTGC	AACCAATTAA	AATAGAAAGG	CTTAAAATAT
	TAATTITGIT				
	TITACTITCT				
	TCTTTCTTCC				
	AGAATGCTTT				
102751	GTAATCACTT	твстттст	TCAAGACTTT	CAAATTTAAG	TAATTTTGTT
102801	TTTCTATTTT	TCATTCAAAA	ATAGGGTTAT	AACATTTCCT	TGACACAAGG
	ATATATATAT				
	CTTGAACTCC				
102951	TGGGATCACA	GGCATGAGCC	ACTGTACTCA	GCCTTTATTA	ATCTAAATAT
103001	GATAATTTAC	CCACTGAGAT	TCATTIGIGC	TGATTAAATT	TACTCTCAAT
	CCCTATATGT				
	TTTCCTTTAT				
	TATGAAGATA				
	ACCTITTATA				
	AGAACATTGA				
	TTAAGTAACA				
	AACCTTAATT GATTCAGGCA				
	GTGGGGATAC				
	ACAAGTAAAT				
	TTCAAAGGAA				
	ACAACTTTGG				
	CATCCTTTGG				
	GACAGCTTTC				
	CTAAGGCCAA				
103801	TGTATTATTA	AAAATCTGCA	TATCAAAAAT	GAAAATGTCT	TGCATACTTT
103851	GCTGTAGGAC	CCAATCATTG	пппспс	ATATACTGCA	TTAATCTGTT
	TTCACACTGC				
	AAGAGGTTTA				
	CATGGTGGAA				
	CAGGGGAGTA				
	TGAGACTTAT				
	GATTTAATTA				
	GAGCTACAAT				
	CATTCTGCCC				
104201	AATTATGCCT	CCACACTCCA	AACTCTCATC	TEACACAACC	CAACTICCCCT
	CTGCCTATGA				
	AATAGGGGTA				
	TGGCCAAAAT				
	GGCAGTCATT				
	CTCACATTCA				
	AAGCTCTGCC				
104701	TCATGGGCTG	GCATTGAGTG	TCTGCAGGTT	TTCCAGATGC	ACAGTGTAGG
104751	CTGTCAGTGG	ATCTACCATT	CTGGGGTCTG	GAGGACGGTA	GCCCTCTTCT
104801	CATAGCTCCA	CTAGGCAGTG	CCCCACTGGG	GACTCTGTGT	AGGGGCTCCA
	GTCCCACATT				
	CCTGCCCCTG				
	CCTCTGAAAT				
	ACCCGCAGAC				
	CCTCTGAAGC				
	GGTGCAGCTA				
102201 TCTCOT	GGGCCACACA	TOCACCCCTA	TEATECEAAC	CCCTACCTT	MACCICIO
	ACATGCCTTG				
	TCTTGTCACT				
	TCCCCAGAAA				
		A			CHICH ICHO





		**			
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		TIGCTATIGT			
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		CAGTTTTGTG			
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TO 30T				GGAACTTGAC	
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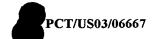
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112351	AGAAGCCTAT	CTTAGGCTGG	GCACGGTGGC	TCACGCCTGT	AATCGCAGCA
112401	CTTTGAGAGG	CCCACCCACG	CACATCATIT	CACCTCACCA	CITICACACC
112401	AGCACGGGCA	ACATTCCTTAA	ACCCCATCTC	TACTAAAAAT	ACAAAAACTA
112451	AGCACGGCA	ACATGGTGAA	ACCCAICIC	CACCTACTCC	ACAMACIA
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	GCAGGAAGCT				
	CTGCCACTGC				
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112801	AGGCAATGTC	ATTGTTGTGC	AAACATCATA	GAGTGTACTT	AGACAACCCT
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	AGGCAGTTGT				
	GTGAAAGTAC				
	CATCTTTGAC				
	TTGATTAGAG				
	TTAGCCGATA				
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	GTCAGTCAGT				
	CTGTCTTGAT				
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	CTCCAAGAAA				
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	CCTGAGGTCA				
	CTCTGCTAAA				
	CCCAGCTACT				
	GGAGGTGGCA				
	AAGACCAAAA				
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	TTTCTATTTT				
	TTAAACTGGC				
	ACATTITACT				
	ACTIGITICIT				
	GTAGAAATAA				
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	TTCTGCCCTT				
	TTCCCAGTCC				
	CATGGAAACC				
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	TTGAATTCCA				
	TTTGATGTAC				
115451	AGAGTTTATT	CTCCTAGACA	TAAAATGAGT	GTACATGCCT	AGCCATTGTC
	CACCOCTTTC				
	AGAGAATCAA				
LUCCLE	~~~		·	-10-10-01	





115601	AATCTTATCT	CCCAAAGAGC	ATAGTTAACT	GCAGCAGCAG	TGGATGATAA
115651	CTACTGGGTG	GGGGTAGAGG	GGTTGTTTTG	CTCAGTTCTG	CCTAGAAGAC
115701	AGTTGTAGTT	ATTITAGTCC	CACAGTCTCT	ACTCCTCCCT	GGGCCTGTTT
115751	TIGOTIGOT	TTCCTGGCCT	CTGTATACGG	CCTTTGTTAG	CACTTTGTAG
		GCTGTTACTC			
115851	TCTTTCAAGA	GTCTCCAGTA	ATCCCCCTTC	TTTTAAACT	ATGACTCCCC
		AGTCTAACTT			
115051	AATAAATTCC	ATAAACCTTA	CATAAAACAT	ATTAAACAAA	AACTACTCAC
110001	AAIAAAIICC	CCACCAACAT	AATCACCATC	ALIAMOVA	CAAATTACAC
TT000T	CCCTTAMA	GGAGGAAGAT	AAIGACCAIC	AAGGCATGGC	CAMATTACAC
		AACAGTACAG			
		TTTGCAGGTG			
116151	TAAATAAAGT	GATTTGGGGT	TCCCTTCTGT	TGAGCATTCT	TCIAICGIGA
116201	AACCATTTGG	TGATGAGAAG	CTTGAGTTTC	TAATGCATGT	TCGTTGGCTT
116251	TATTGGAGCT	GCTTTTGTAC	TGTGGCCACC	CATTTAACTT	ccrcrarear
116301	TGATATATGA	GAGCTAGAGG	ACTCTGCCTT	AGCTTCTTCA	TCAGAACACC
116351	ATGTGATGTC	TCCAAATGTC	TTACACTGTG	GCTCCCCTGT	AAGAGAGGTG
		AGGCCAAGGC			
116451	TTAGGCTACT	GCCTGAGACC	TCTCAAACAG	GATCTGTCTG	TGGGCTCTAG
		GTAACCGGCC			
		TGGTGGCTCA			
116601	ACCETTECACE	ATTGCTTAAG	CCCACCACTT	TEAGACCAGC	CTGGGCAACA
116651	TAACACCACC	ATGTCACTAC	AAAAATGATT	TAAAAATTAG	CTCCATCTCC
116701	TOCCATOTAC	टावाब्वाव्व्	ACCITACTICGG	CACCCTCACC	TACCACCATT
110/01	TUGCATGTAC	AGGAGGTCGA	ACCUTECACTIC	ACCTICACT	CCCCACTCC
TT0/2T	GITTAAGCCC	AGGAGGICGA	CTCAAACTCT	CTCTCAACAA	CAAAAAATCT
TT080T	ACTCAAGCCT	GGGCAACAGA	GIGAAACICI	GICICAGAA	GAMMAAIGI
116851	TTCAGGCACA	GTCAGTGTTG	AAGAIGICAA	TIAGCAAGGI	IIIIIIAAIC
		GTGCAACCCA			
		TCCTGGCCGA			
		CTGAGGCAAG			
117051	CCTGACCAAC	ATGGTGAAAC	CCCGTCTCTA	CTAAAGATAC	AAAAATAAGC
117101	CGGGCGTGGT	GGCGGGCACC	TGTAATTCCA	GCTACTCAGG	AGGCTGAGGC
117151	AGGGGAATTG	CTTGAACCCG	GGAGGCGGAG	GTTGCAGTGA	GCTGAGATCA
117201	TGCCACTGCA	CTCCAGCCTG	GGTGACAGAG	TGAGACTCCA	TCAAAAAAA
		AGATGAATTC			
		AAAGTTAACT			
		GACAGTGACC			
		TATGAAAACA			
		AATATCCATT			
117501	AGTGCATGCC	AGTCTCCAGA	GGATGACAGA	TGGGCAGAAA	TTTATAAAAC
117551	AGCAGCAGTC	ATGGACAGCC	TAGGCCACAA	GTAGAACATA	CCAGACCTCC
117601	TECETACTAC	TGTCTCAGTG	AGAAAGGATC	CAGAGATICCA	GCATCACCAG
117651	ATTICCTCAC	ATACTGACCA	AAGAAACTTT	THAGITIG	AGATTTIGGT
		AGGAGTATTA			
		AACAAAATTC			
117001	TCATGGCAGT	TGCACTTTAG	CAACCCCAAC	CACCCACATC	ACTICACCITC
117001	ACCACTE	AGACCAGTCT	CCCCAACTTC	CTCAAACTTC	ATCTCTACTA
11/901	AAAATACAAA	AATTAGCTGG	GCGIGGIGGI	GCACACCIGI	AATUUAGU
11/951	ACICIGGAGG	CTGAGGGAGG	AGAATUGUTT	GAACCAGGIA	GGTGGAGGTT
		GAGATCACAC			
		AATAAATAAA			
		TTGAAAAACT			
118151	CCCAATTTAT	CTTCTTTCAA	AATACCTCAA	ACATTTCACC	TTATTATTCT
118201	TTTTAAGGAT	TACAAAGTAG	AGCAGGGGGG	AAATAATAAA	CCACTAATAA
		CCATTTGACA			
		AGATTCAGTC			
		GGAGACAGGT			
118401	GAACATAGGT	TAGAGGGGAG	AGATTTAGGA	GTGAGGGCTC	AAGCAAGAAG
118451	CATGTTAGAA	GACTGCTGTA	GTGGTCCCGG	TGAGGAGTGA	AAGGAATGGA
					CTGAGAGATT
	ACTAAAATAC	CAIGARAME			
			TTCAGTGGTG	ACTICITICAT	TTGAAGAGGG
118551	TAGAAAGTAA	ATCATCAGGA	TTCAGTGGTG	ACTICTIGGAT TCTGCCATICS	TTGAAGAGGG
118551 118601	TAGAAAGTAA AAAGGGAATA	ATCATCAGGA ATCTAGGGTA	GCTGTCAGTT	TCTGCCATGG	GTAGTTGGGC
118551 118601 118651	TAGAAAGTAA AAAGGGAATA TAACAGTAGT	ATCATCAGGA ATCTAGGGTA GTATTAACTG	GCTGTCAGTT AAATGGGGGG	TCTGCCATGG CAGGCAATTT	GTAGTTGGGC GTGAGGGTGA
118551 118601 118651 118701	TAGAAAGTAA AAAGGGAATA TAACAGTAGT GTTGAGTTCA	ATCATCAGGA ATCTAGGGTA GTATTAACTG GCACAGGGCC	GCTGTCAGTT AAATGGGGGG TGTTGACTTT	TCTGCCATGG CAGGCAATTT GAGGTGCCTT	GTAGTTGGGC GTGAGGGTGA TGAAACAGGA
118551 118601 118651 118701 118751	TAGAAAGTAA AAAGGGAATA TAACAGTAGT GTTGAGTTCA GTGGATATGT	ATCATCAGGA ATCTAGGGTA GTATTAACTG GCACAGGGCC CTAATTTTAC	AAATGGGGGG TGTTGACTTT ATGAAGTGTC	TCTGCCATGG CAGGCAATTT GAGGTGCCTT TACTTAAGAG	GTAGTTGGGC GTGAGGGTGA TGAAACAGGA AATGTGTAGA
118551 118601 118651 118701 118751 118801	TAGAAAGTAA AAAGGGAATA TAACAGTAGT GTTGAGTTCA GTGGATATGT GACATTAACA	ATCATCAGGA ATCTAGGGTA GTATTAACTG GCACAGGGCC CTAATTTTAC GGGCTGGGTA	AAATGGGGGG TGTTGACTTT ATGAAGTGTC GGAACACGGA	TCTGCCATGG CAGGCAATTT GAGGTGCCTT TACTTAAGAG ATACCTCAGG	GTAGTTGGGC GTGAGGGTGA TGAAACAGGA AATGTGTAGA TGCCAAATGA
118551 118601 118651 118701 118751 118801 118851	TAGAAAGTAA AAAGGGAATA TAACAGTAGT GTTGAGTTCA GTGGATATGT GACATTAACA AAACTTTTGG	ATCATCAGGA ATCTAGGGTA GTATTAACTG GCACAGGGCC CTAATTTTAC GGGCTGGGTA CAATAACAAG	GCTGTCAGTT AAATGGGGGG TGTTGACTTT ATGAAGTGTC GGAACACGGA AAGTTAGGAA	TICTGCCATGG CAGGCAATTT GAGGTGCCTT TACTTAAGAG ATACCTCAGG GTTGAAGAGG	GTAGTTGGGC GTGAGGGTGA TGAAACAGGA AATGTGTAGA TGCCAAATGA GTAGAAGAGG
118551 118601 118651 118701 118751 118801 118851 118901	TAGAAAGTAA AAAGGGAATA TAACAGTAGT GTTGAGTTCA GTGGATATGT GACATTAACA AAACTTTTGG CAGCAGAAAT	ATCATCAGGA ATCTAGGGTA GTATTAACTG GCACAGGGCC CTAATTTTAC GGGCTGGGTA CAATAACAAG GTAGATGGAT	GCTGTCAGTT AAATGGGGGG TGTTGACTTT ATGAAGTGTC GGAACACGGA AAGTTAGGAA AAGAACATGT	TICTIGCCATIGG CAGGCAATTT GAGGTIGCCTT TACTTAAGAG ATACCTCAGG GTTGAAGAGG TIGGCATGTTT	GTAGTTGGGC GTGAGGGTGA TGAAACAGGA AATGTGTAGA TGCCAAATGA GTAGAAGAGG





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119001	GCAGGCCTAA	TGCAGTTTGC	AGACGTGTTT	TGTTAGACTT	TTGTAGAGCT
119051	GGATCACACA	GTGTCCTAAA	TTTAAATTAG	GTGCCAACAT	TTCCACACAA
119101	AATCCGGATT	TCTGACTTTT	CTTTTAAACT	AAAGGGCTCC	TAGAGGTAGA
119151	TTTGGCAACA	TTGGTAGACC	TATATGATAA	TAATCGACTG	AAGTATATGT
	CCTTTCTCTC				
	AGACATTTAA				
119301	ATGAATITIC	TACTTCTGAG	TCAAAGATCA	GTAGGTAATA	AAGGTACAAA
119351	GATAGATTAG	CAACAGATTA	CGGAGAGCTT	TGAATACCAA	TCTAAGGAGT
119401	GTAAATGTAG	GCAGTGGGCC	ACCTUGAAT	AAGGAATTGA	TGAGATTAAA
	GCCATATTTA				
110501	GGAAAACAGT	TAATAGTTTT	GAAAGAGAAG	AGAAAAAGGA	GATGGTGTTG
	GGATACATAA				
	ATATCACCCA				
110651	TGTATTTGGT	CCCAAATTTC	CTTCCACACT	TOCACAACTIC	AGACCAATGT
110701	GIGGIGIGG	CCACCCTCAT	TETCACCCAT	TATICGAAACG	TCAAACAAAA
	TATGCTCACT				
	AGTACACTAA				
	TAATACCTGA				
110001	ACACACACAC	TIGHTALIAA	CIGIGIGCCA	AATTECTCAA	CTACCTACTT
	ACACAGACAT				
11332T	TTCCAATTTC	CATITIACAG	ACAGAGAGAC	IGAAACCCIA	GAGGITAAGA
15000T	AGTTATCCAA	AGCCACAAGG	CIGAIAAGAA	CAGAACCAGG	ACTIGAACGC
	AAGCAGTCTG				
	CCCCTGCATT				
	GTAGAGGACC				
	GGGTGTCAAT				
	GACCCTTGAA				
	GACCTTGAGA				
	ATGGATCAGT				
	TAAAAACTCT				
	CTCTGTCGCC				
120501	CTGCCTCCCG	GGTTCAAGCT	ATTCTCCTGC	CTCAGCCTCC	CGAGTAGCTG
120551	GGATTACAGG	CATGCGTCAC	CACGCCTGGC	TAATTTTTAT	ATTTTAGTA
120601	GAGATGAGGT	TTCACCACGT	TGGCCAGGCT	GGTCTCGAAC	TCCTGGCCTC
120651	AGGTGATCCA	CCCACCTCGA	CCTCCCAAAA	TGCTGGGATT	ACAGGCGTGA
	GCCACCATGC				
	GTTAATTTTT				
	TAAATATTGA				
	CAAATGCATT				
	TCAGTGTGGT				
	GATTTCAAGA				
	ACTICAGGAG				
	TGGTGTGAAG				
	TATCAAAAAT				
	CTTANATICT				
	TCTTATTGCC				
	CTCCACCTCC				
	TGGGATTACA				
	AGTAGAGATG				
	CCTCAGGTGA				
	ATAAAAATGA				
	AAGGACAAAA				
121561	TGAAACAACA	ATTICITIES	dilligggiii	AACTCCACCA	AACCACAATC
121501	GTTTTCATCC	ATTOCTOT	CTATCAACAA	TCTTTTCC	TOTACTO
	ATAGTCATGT				
	GIGIGIGA				
	GGGGTGAGCA				
	AGAACAGGTA				
	GAAGACTTAA				
	TCATGGGAGA				
	CTAGATGAGT				
	AAGGGCTGAG				
	ACAGAGAAGC				
	CACTGTGGAG				
	ATGGAATAAA				
122201	AGCAGCTTGG	GAAGGGCGGT	TATGTACATG	AGCTCTATCC	TGCAATCTAC
	TAGGAGCTAT				
	CCCCCCTTCC				
122351	CAGGCTGGAG	TACAGTGGTG	CCATCACAGC	TCACTGCAGC	CTCAACATCC





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122401	CGGGCTCAAG	CAATCCTCCC	ACCTCAAACT	CCTGAGTAGA	TGGGACTACA
122451	GGTGCGTGCC	ACCATGCCTG	GCTAATTTTT	GITTITIGI	TTTTTTCTG
			GTTGCCCAGG		
			AGCCTCCCAA		
			TGTGTTTTAT		
			ATCCCAGCAC		
			TTTGAGATTA		
			ATCCAGGCAT		
			AGCAGGAGAA		
			TTGTGCCACT		
			GAAAAAAAAA		
122951	AAGAGTGGAA	TGGAGTGGAG	GAGGGGACAA	GAGTTGAGAT	AGTCACAAAA
123001	GGCCACATAC	TGAATGATTC	CATTTATATG	AAGTGTCCAG	AATAGGAATC
123051	TCTGTCTCTT	TCCATAGAGA	AAGAAGGTAG	ATTTGTGGTT	GTAGGGGCTA
			GTAACTGCTA		
			GATAGTGATG		
			AGAATATGAA		
			GCAGCTCATG		
			CACTTGAGGC		
			CTACCAAAAA		
			CCTATAGTCT		
			GGACTTTGAG		
			GGTGACAGAG		
123551	TTAGAGAAAA	AGAGTAGAGG	TCCAGGGACT	AGTTGGAAAC	TATATTAAAG
123601	TAGTCTAGGC	ATCTAGGCAG	GAAGAACCAA	GGCAGAGATA	CTGAGATCAA
			AGAGAATGAG		
			CTCAGGTAAT		
			GTAGATCTAA		
			TTTCACCCAA		
			IGIIGIIGI		
			AAGAGTCTGG		
			CCTGTGGGTT		
			AGATGGAAAG		
			GTTTCTAGGG		
			GCTGAAAGGT		
124151	GGAGGCTATG	AGTGAGCTTA	CAGAGAATGG	TTTCTACAGG	TGCAGAAAAT
			AATGGAAATA		
124251	CTTGGCTGTG	GAAGGAAGGT	AAAGGCAAGC	CACAAGGGGG	GGTCTTAGGT
			AATTATATTA		
124351	AGCAGGGCCT	TGAAAAAGAG	GTGAAATTTG	GACACAGGAA	AATGATTGGA
			TAACTTCCAT		
			ACTITICATIGT		
			TGATCCTTGC		
			TTAGAGATGT		
124501	CCTACCTCAC	TOTAL	TGTGTGTATA	CACCTICACC	CACTICACACC
124001	ACACTE CAL	CACACACCTA	GAAGGAAGTG	AACACACTEC	CTAATCTCCT
			TGTATCATGA		
			ATTTAGTTTT		
			GCACTACAGA		
			GCCCCAAGCA		
			ATGGTCCCTG		
			GTGTGGAAAC		
			GTTAGAGTGG		
			TTTGCTTTAA		
			AACCCCAGCA		
			TCGAAACACA		
			GGCTTGGTGG		
			GAGAGTCGCT		
			CTACTGCACT		
			AAAAAAAGT		
			TAAAGTCACT		
			AACAAGAGTG		
			CCAGGTGAGA		
			TATTTTATAT		
125601	CAATGTTTGA	ACGTCCTCCT	ACCCTAGATA		
125651	ACATTTTTGG				
125651 125701	ACATTTTTGG AGAAAATATA	GCCTTTCCTA	ACTTGTCCCA	TGTTGGTCTG	CAGTTACACA
125651 125701	ACATTTTTGG AGAAAATATA	GCCTTTCCTA		TGTTGGTCTG	CAGTTACACA





125801 AAGTITAGCC ACAATCTGGC TTCTGTTAGG CCTTATCTAA TTTTTGCATC 125851 CAAATGTAGA GCATCGTTTG TGGCACCCAG TAGCACATGC TGAGTCACAG 125901 GTGTGACAGC TGCATTTCAA ACAAGCCTGA GAAGGAGAAA GAAAGCCCTT 125951 CAGTGTGTCC TGTGGTTGCG AGGAGCCACT CACGGACTCC ACCTTGTGAA 126001 CACAGCGGCA CAGGACGCAA CACAGGCCTA ACCCATGCAG GATGCTGGAC 126051 TCGTTCCCTT ATTCACTACC TCCTCTCTCT CCTTTTTCAT GGCTTCCTTG 126101 CCCCAACATC CCAAACACAC AGTGTGGTTT TTGATTCTTG GCTCTTCTCT 126151 GCTGCAGTTG ACTCCAGCTC TGCCTGTTTG TTCCTTCCTT TTTCTCCATC 126201 CCTGGCTCTC TGCCTTTTGG CCCATCCTTT AAGGCTTGGA ATGCTCCTGG 126251 GCTTACCTTC TTTCCATTCA TTGGTGGTGT GTTTTCTCAG ACATACCTGC 126301 TCCCTGCTTT CATCTTTCAA CTTCTTGGGG CTGTGACAAC TCTTCCCTCT 126351 TTGTCCCCTG GAAGCCAGTT CTGAGTAGCA GCCAGGCCTA GAACACTGGT 126401 GACACAGACA CACTTCATAG CCCTCCCGCA TGGTCTAGTT TCAGATCATG 126451 GTAATCCCTA GTCTAGGAGG CTGCCGAGCC CAAGAGCACA GGCTCTGGAG 126501 TGAGAAGCCA GTTCACCCCA GTTCTACCAC CAACTTGAGA ATCAGCAGAG 126551 GGCTGTGGTG AGGATTCTTG GTGGCAGGTT ATGTAAAGTG CCTAGCCCAG 126601 ACTGGATGAT TAATAAATCC TTGCATCTGT TATGTTTTAA TATCTTATTA 126651 AATACTGAAA GCAGATCCTG ATTTGGAATA GGTCTCAAGA AAGGAGACTA 126701 GGGTCTAATC CTGAATTAGA GTCTTTGCTT ATAGGTAACA AAGAATTTAT 126751 GAATTTATCT CACATTTTTG CTTAAGAGTT CTGAATTTAA ACTTCCATCA 126801 AGGTOCTGGG TCCCAGGTGT TTTCAACCTA ATAATTCTAA ATATTGAGTG 126851 GTTGGTTGCA GTAGCTTATG CCTATAATCC CAGCGCTTTG GGAGGCCAAG 126901 GCAGAAGGAT CCCTTGACCC CAGGAATGCA AGACCAGCCT GGGCAACATA 126951 GTGAGACCTC ATCTCTACAA AAAATTAAAA AGTTAGCTGG ACATGGTGGC 127001 CTACACCTGT AGTCCCAGCT ACTTGGGAGA TTGAGATGGG AAGATTGCTT 127051 GAGCTGGGGA GGTTGAGGCT GCAGTGAGCT GTGATCATGC CACTGCATAC 127101 CAGTCTGGGT GGCAGAGTAA GACTTTGTCT CAAAAAAATA AAAAAATAAA 127151 AAAAAATGCT GAGTCAAGTC TACTGCTCCT GCCAGAAGAG ATGACTGAAG 127201 TGCATTACGT AGAATAATAA TGGTTAAAGA AAAGCTTTGC AAAAGTTCCC 127251 AGAATATATA CTTTATTGGG ACAGGAGAAG CTACGTGTGT CGTGGTATCT 127301 TITTACTATT TICTTAATCT TATAGGCCTG TGTTTCTAGT CACCATTAAA 127351 TTACTACAGA TTTGTGTTTT TAATGTAATA TATAAGTGTT TTGGAAGGGT 127401 GAGAATATTT CAAAGGTTTG AAAGTTAAAA CTGTGTATGA AAGAATTGAA 127451 AACTIGGAAT TTAGATCACT TTTCCATTGT GTCATATTTC TCTGTGACAT 127501 GGACATATTG AAGCATGGAC ATCATGTCCA TGCACATAAA GCAGACAACC 127551 CAGACAACAC ACACATGTGC ACAGGAACGC TCTGGAAGGA TGCAAACCGA 127601 ACTGTTAAGT GTTGATTCCT GAGGAGGTGA ATGGGCATGG GTTGAGAGTG 127651 AGAAGAGGTT GTAGGAAGAC TTTCATATAT TACTGTGTAC ATTTCTCTAA 127701 GGTTTGAATT TTAAAAAATA TATTCATGAG TTACTTTTGT AATGTAGAAA 127751 TATTAATGAC TITICCTATCC ATCAGTCTGC CTAAGCTTCC TCTTCCGGTT 127801 CAGGTAGAAT GAATTGGATC AGTGTTGCTC CATTTTCCAT TTTAGCATTT 127851 TACATTTGCC TAAAGATATC TTGGGATGAG GGTATATACT TTATCAAATG 127901 TAAGCTATTT CCAAAGTAGT AAATCCAAAT ACTTAACAAC TTCCCAGCCT 127951 AAGTAAATGA TCAGAGGCTC CGTACTCAGT CTCATCTAGA CTGTGGCACT 128001 GGGTGTGAAC GTATCAAATG CATGTTTCTC CATCAGGCAG AAGTGAGAGT 128051 AACCATGTGC CATGGAGAAG GTTGACAGAC TCCCTGTGAA GCACTTCGAA 128101 GTGACACTGG CCTCTGTGTG CTTCAGAAGA ATCCAGCCAC CTGCTGTGTG 128151 GCCTGACATT TTCCTTTAGT TTGTGATGGG CCAGCAGAAC TCTGTTGCCA 128201 ACTGTTTTCT GTCCTGGGTG CCTAGCCAGA GGTTCTGAAA GTCTGGAGAC 128251 TITATATIGG CTAAACTITA GGAACGICAA TTACATGICT ATCTCCAAGA 128301 TGCCTTCTTT TATTCAGGTG CAGCTCATTG TTTCCTCTTG AGCTACACTT 128351 AAGATTCTTG AGCAAAACCT AAACTGACAT TTCTCCAGCA ATGCTCTCCT 128401 TGAGATAGAA ATGGGAAAAG TAAGAGCAAA AGGAATCTTT TGTTCTCATG 128451 TGCATACACT AACTCATAGA AGGTTAATAC TTCTATAGCC TGTACTATTA 128501 TAACAAGTAT TATATATTTA TGATATATTT CCTTAAAGAA AACAAAAGCA 128551 ATATAGACAT CTAAACTGTC ACTGGCTTAT TAAGTGTCAG TGCCAGAGCC 128601 TAGGAGAAAA TAAGGAGCCT GTGAATTCCT TACTCGAATC TAACCAGAGC 128651 TGCTGTGTTT GAGAGCAAGT TTTAAAAGAT TGTATGTAAT ACTAAGTTTA
128701 TTCATCTTTC ACACTGAGTC CCAGCATCAC CAGATCAGTA TTTGATGCCT
128751 GGATCAATCT TTATTCTGGG GAGTGATGAA GCATTGAACC TGCTATATGT 128801 ATAGTTTGCC GAGCGTCGGC ATGTGCTCCT TGTGGCCCAG GCATCCCTGC 128851 ATATAAGGAA TAGGTACGTT CTCACGAGCC TCACCTACTT ACCTCCACAT 128901 TTAGCCAGAT TCTGGGTATT AACATCTGCT GGGAAAGAGC ATCACTACAG 128951 TAGCTACAAA TAAGGTGGAA GAAGCAAAGT ATTTTTCTGA GAAGTACTTA 129001 AAGAATAGAT GTGTAAATTT CTATAAACAC AAGTCTTAAA GGAAAATGAA 129051 AAAATTITAC ATITAAATAA CTACATAAAT CATTGCCTAA TTITAATAAG 129101 AATATAACTT AATATAGCTT GAATGGAGAA AAGGACAACT TGCAGTCAGG 129151 GAAAGTATTA AGAAATAATA TIGCTCAGTICT GGGCGCGGTG GCTCATGCCT





129201	GTAATCCCAG	CACTTTGGGA	GGCCGAGGCA	GGCAGATCAC	GAGGTCAAGA
129251	GATCAAGACC	ATCCTGGCTA	ACACAGTGAA	GCCCCATCTC	TACTAAAAAT
120301	ACAAAAAAGT	ACCCACGCGT	CCTACTCCCC	GCCTATAGTC	CCAGCTACTC
120251	GGGAGGCTGA	CCCACCAAAA	TETTETCAAC	CTCCCACCCA	CATCLICCAC
15322T	GGGGGGGG	GGCAGGAAAA	10110104AC	CIGGGAGGA	GATCHIGOAG
129401	TGAGTCGAGA	TOGOGCCACI	GCACTCCAGC	CIGGGIGACA	GAGCAAGACT
129451	CCATCTCAAA	AAAATAAAAA	AAATAAAAA	AAGAAATATT	ATGCTCAAAA
129501	TATATAGCAA	TAAGTTGGAA	ACTITIACTI	GAATAATTTT	TACAAAACTG
120551	ACCAAAGAAC	AAAAACETGA	AGAGGCCAAG	TTCCAACACT	CATCHTATCE
17900T	AAATTGTTCT	AAAACAACAI	TAGCACTTAA	CAVAGI IGAA	AAGI TAACAA
129651	AGCCAAGTAC	TGTACTAGGC	TTCCAACACT	AACTAAGTAT	AAAATTCCAC
129701	AGAGCTGGTT	TTCTTATCTT	TAAAGAAATT	TGTTGGCAAG	TGGTACTGGT
	GTTAAAAAAA				
	AAATATGAAG				
129001	AMIAIGMG	CACATTAWA	CCCA ATTENTIA	CTCTATACT	ATTA A CA A TT
T5882T	ATAATTACAG	IGGCAIGGII	GGGAAIGIII	GGICIAIAGI	TTTAACAATT
129901	AAATCCATTG	AATCTGGCCC	CGTACCATCC	TAAAGTTTTA	TTCTAGATTC
129951	TCTGGAGTTT	GTGATTATAG	ATATGTTTCT	AAGATTTAAG	TAACTTTCCA
	TGTTTATCTC				
	AAGAATATTA				
	TGGGAGGCCA				
130151	CTGGGCAACA	TAGTAAGACC	CCATCTCTAC	AAAAAAATAAAA	AAATTAGCCG
130201	GGCATAGTGG	CATGTCCCAG	CTACTTGGGA	GACTAAAGTG	GGAGGATCAC
	TTTGAGCCCA				
	TTCCAGCCTG				
	GTTTATCTAC				
130401	CITGITAATT	TCAAACCCCTT	TTCTACATTT	TGATTTATCT	TTAAATCTCT
130451	TTTTGTCTCA	ATAAATGGGA	AGTATCAGGA	AGTCTTTTTA	CTTGCTCAAG
	GTCATAGAGA				
	CCAACCTGCC				
	GCTTGTGCTG				
130651	AACAAAAGTC	AGGAGAATGG	GGAGATTTTG	TTCTTTTGAA	ATGCTAGTGT
130701	GAAGTGCTAG	GCTTATTTTT	CAAATGCCCA	ACTOGTATIC	тттстттс
	пппппп				
				CTGCTGGGTT	
130851	TCCTGCCTCA	GCCTCCGAGT	AACTGGGACT	ACAGGCGCCC	ACCACCACGC
130851 130901	TCCTGCCTCA	GCCTCCGAGT	AACTGGGACT TTTTGTATT	ACAGGCGCCC TTTAGTAGAG	ACCACCACGC ACGGGGTTTC
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130851 130901 130951	TCCTGCCTCA CCGGCTAACT ACCGTGTTAG	GCCTCCGAGT TTTTTTTTT CCAGGATGAT	AACTGGGACT TTTTTGTATT CTTGATCTCC	ACAGGCGCCC TTTAGTAGAG TGACCTCGTG	ACCACCACGC ACGGGGTTTC ATCCGCCCTC
130851 130901 130951 131001	TCCTGCCTCA CCGGCTAACT ACCGTGTTAG CTCAGCCTCC	GCCTCCGAGT TTTTTTTTT CCAGGATGAT CAAACTGCTG	AACTGGGACT TTTTTGTATT CITGATCTCC GGATTACAGG	ACAGGCGCCC TITAGTAGAG TGACCTCGTG CGTGAGCCAC	ACCACCACGC ACGGGGTTTC ATCCGCCCTC CGCGCCCAGC
130851 130901 130951 131001 131051	TCCTGCCTCA CCGGCTAACT ACCGTGTTAG CTCAGCCTCC CGGCCAACTC	GCCTCCGAGT TTTTTTTTT CCAGGATGAT CAAACTGCTG GTATTCCTAA	AACTGGGACT TITTIGTATT CTTGATCTCC GGATTACAGG ACGAATCATA	ACAGGCGCCC TITAGTAGAG TGACCTCGTG CGTGAGCCAC ATTITACCAT	ACCACCACGC ACGGGGTTTC ATCCGCCCTC CGCGCCCAGC AAGACCATAG
130851 130901 130951 131001 131051 131101	TCCTGCCTCA CCGGCTAACT ACCGTGTTAG CTCAGCCTCC CGGCCAACTC TTTAGTGATT	GCCTCCGAGT TTTTTTTTT CCAGGATGAT CAAACTGCTG GTATTCCTAA GAAGAAAAAA	AACTGGGACT TTTTTGTATT CTTGATCTCC GGATTACAGG ACGAATCATA TGTACCGAAC	ACAGGCGCCC TITAGTAGAG TGACCTCGTG CGTGAGCCAC ATTITACCAT TGTATGATAT	ACCACCACGC ACGGGGTTTC ATCCGCCCTC CGCGCCCAGC AAGACCATAG GATGGTGTCA
130851 130901 130951 131001 131051 131101 131151	TCCTGCCTCA CCGGCTAACT ACCGTGTTAG CTCAGCCTCC CGGCCAACTC TTTAGTGATT AAAAGAACTA	GCCTCCGAGT TTTTTTTTT CCAGGATGAT CAAACTGCTG GTATTCCTAA GAAGAAAAAA ACCCAATATG	AACTGGGACT TITTTGTATT CITGATCTCC GGATTACAGG ACGAATCATA TGTACCGAAC AAACAGTTTT	ACAGGCGCCC TITAGTAGAG TGACCTCGTG CGTGAGCCAC ATTITACCAT TGTATGATAT CAGGAGCATG	ACCACCACGC ACGGGGTTTC ATCCGCCCTC CGCGCCCAGC AAGACCATAG GATGGTGTCA TTTCCTATTT
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130851 130901 130951 131001 131051 131101 131151 131201 131251 131301 131351 131401 131451 131501 131551	TCCTGCCTCA CCGGCTAACT ACCGTGTTAG CTCAGCCTCC CGGCCAACTC TTTAGTGATT AAAAGAACTA TGGTGTCAGT ATTCCACCCA GTGGCTGCCC GTGTGCTAGT TACAGCTGCT TACAGCTGCT GAGGGCACCC GGGCCATGGT CTCTCCCAGC	GCCTCCGAGT TTTTTTTTT CCAGGATGAT CAAACTGCTG GTATTCCTAA GAAGAAAAAA ACCCAATATG GAACTCACAC CGAGGTGTAC AGGGCCTAGG TTATCTGGTC TCCAGGCACA TCCAGGACGG GTCACTATCT	AACTGGGACT TTTTTGTATT CTTGATCTCC GGATTACAGG ACGAATCATA TGTACCGAAC AAACAGTTTT TGTTAAAGTT TCTGCACCTT TACCAACCTC AAAAACAGAA TCTCCTTCCT GTTCTTCA TCATCAGCAA	ACAGGCGCCC TITAGTAGAG TGACCTCGTG CGTGAGCCAC ATTITACCAT TGTATGATAT CAGGAGCATG GTGAAAACCA CAGAGGCCCT CAGCTTCCGT CAGCTTCCGT CAGCCTGCTG CAGCCTGCTG TGTGCCTTTGG AATGGAGATA	ACCACCACGC ACGGGGTTTC ATCCGCCCTC CGCGCCCAGC AAGACCATAG GATGGTGTCA TTTCCTATTT ACACTCCTGA CAGATTGTGA AGGTCCGTAG CAGTGATGCA ACTGCTATTG CTGCCCCCGT GCACATTAAC ACATTAGTAC
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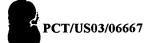
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132751	ACTAAAAATA	CAAAAATTAG	CTGGACTTTG	TGGTGCTTGC	CTGTAGTCCC
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			ACACCACTGC		
			CAATACGTTT		
			TAGGGGAACT		
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133051	AGGGGGAACC	AGTAATGACT	TAGAAGTCCT	AAGCATGTTG	CATGGTAATT
133101	GTGACATTTG	CTTCCTGCGA	GCGGAGCTGA	CCTTGTGGTG	TCCGTCCTAG
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133451	ATTTATATAT	AAAACATATT	ACAGGTTATT	GATTACTIGGT	CITICAL
133501	TATIGICAL	TTACTIGATAA	CATTTTTAAT	AAGACTAGCT	ATTAAACAGT
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			CAACATAGTG		
133701	ATAAAAAATA	AAAAAATTAG	CCAGGCGTGG	TEGCATECAT	CTGCAGTCCC
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122001	TOCCOTION	CTAACACATC	ATACATCCCC	CTGAGGAGTA	CTTCATCAAA
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			ACCAGGTGAA		
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124101	CIAMOIGAM	AATTCCCAGCA	CTTTGAGAGG	CCVVCCVCC	ACAATCATTT
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			AAAATAGGTA		
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			TIGIGIAIGI		
			CTATTTCATG		
			GATGTCCTAT		
			AGATTCAGTA		
			TTTGGCACAT		
			CCTGAACTGT		
12/001	CAACCACACT	TACTACTEAG	CAGACCAAAT	CACTITANG	TTCAAAACCT
124001	CATCCTCTCC	TTATACCACA	ACCCTCCATT	CCTTCTTCTC	TCCCCCACCT
132001	AATATACTAT	TOTAL	TTCTATAGCC	TACAAGCTTA	GITTATAGE
132001	TTCTAACTCC	ACACCAGATT	TTATATAAGC	ACCACTICTAG	TAGTAAATAG
132101	TTTTCTACC	ACAACTICACA	GTTAACAGAG	CAACAATAAC	CCACCTAACA
132121	CCAAACTICT	AAAGCAGGCA	GAACACCACC	ACACAGCAAC	TCCCACCACA
132301	AACCTCCTCC	CTCACCACCA	GGCTCTGAGG	CCATCATACT	ATTACACCAC
			TAAGGAGGAA		
			GCATTTACAG		
			THAIGIGH		
132401	CTCACCTATT	TATTTAACAA	TGTCAGATAG	ATATITACTA	CACTATATTC
132461	CCTCCACATT	TTAGATAACT	TAGGTTTTAT	ACTATANCIT	ATAAGAGITT
132201	AAAAACACTA	ACATAACTTT	TAAAACCATG	VCICCIOCVA VCICCIOCVA	TITICITACAC
136661	ALJAJAVAVA	TOTTOACTAC	CGTAAAAGTT	TTCACAACCA	GAACCCCAAT
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125701	CAAATTATTA	ACTATION	TTTTCTTAAT	TTTCAATTAT	CATCLTAAAT
		~~\!!!\ ~~~\ !	AAAAAAAAA	ACACCAAACA	STIGITISMI
135701	ACTITION TO	TTATTYCATA			(-10(-) 1 1 (-0 A
135751	AGTTTTCATG	TTATTTCATA	CCCTCTAATC	TCACCATTTT	CCCACCCTTCA
135751 135801	AGTTTTCATG AGCTGGGCAT	TTATTTCATA	GCCTGTAATC	TCAGCATTTT	GGGAGGCTGA
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135751 135801 135851 135901	AGTTTTCATG AGCTGGGCAT GGTGGGAGGA GACAAAACCC	TTATTTCATA GGTGGCTCAT TTGCTTTAGC CATCTCTACA	GCCTGTAATC CTAGGAGCTT AAAAATATAA	TCAGCATTTT GAGACCAGCC AAATTAGCCA	GGGAGGCTGA TGGGTAATGT





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Feature:

Start: 2104
Exon: 2104-2446
Exon: 87054-87198
Exon: 91571-92024
Exon: 120932-121075
Exon: 133151-133379
Exon: 136340-136569

Stop: 136570

Sim4 results:

Exon: 2104-2446, (Transcript Position: 1-346)
Exon: 87054-87198, (Transcript Position: 347-491)
Exon: 91571-92024, (Transcript Position: 492-945)
Exon: 120932-121075, (Transcript Position: 946-1089)
Exon: 133151-133379, (Transcript Position: 1090-1318)
Exon: 136340-136572, (Transcript Position: 1319-1551)

SNPs:

DNA Position	Major	Minor	Domain	Protein Position	Major	Minor
352	A	G	Intron			
381	C	Ť	Intron			
3505	Ğ	À	Intron			
10280	Ğ	СT	Intron			
11107	Ğ	Ā	Intron			
15750	Ť	c	Intron			
16004	Т	Ā	Intron			
16871	A	G	Intron			
17163	T	Č	Intron			
17966	Α	G	Intron			
19392	C	G	Intron			
20113	Т	C	Intron			
20434	G	Α	Intron			
21243	Т	G	Intron			
23009	С	Т	Intron			
24699		T	Intron			
28058	Α	Т	Intron			
29600	T	C	Intron			
31455	Α	G	Intron			
35653	T	C	Intron			
42700	Α	G	Intron			
45516	G	Α	Intron			
51789	C	T	Intron			
52042	C	Т	Intron			
52139	T	C	Intron			
53089	Α	Ċ	Intron			
53117	C	Α	Intron			
53434	_	TC	Intron			
55431	T	G	Intron			
55905	C	T	Intron			
60567	C	Т	Intron			
60751	C	T	Intron			
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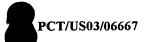
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84331	A						
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86175	Α	-	Intron ·				
87109	C	Т	Exon, coding	133	1	V	V
89444	Α	T	Intron				
90535	G	ATC	Intron				
91163	Ť	A	Intron				
93488	À	2	Intron				
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96065	Ţ		Intron				
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96701	Т	C A	Intron				
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97648	G	T	Intron				
97814	Α	G	Intron				
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103926	C		Intron				
107845	C	<u>T</u>	Intron				
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110188	Α	TCG	Intron				
111006	C	TA	Intron				
111223	A	G	Intron				
111457	T	Č	Intron				
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114155			Intron				
	-	<u>A</u> T					
114181	-	<u>T</u>	Intron				
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115964	Α	C	Intron				
118100	-	A G	Intron				
119631	Α	G	Intron				
120833	Т	C	Intron				
121125	À	Ğ	Intron				
121245	Ĉ	Ť	Intron				
121521	Ğ	Å	Intron				
124296		Ť					
124290	C		Intron				
124549	G	<u>A</u>	Intron				
124858	G	Ţ	Intron				
125920	Α	Ŧ	Intron				
126266	Α	G	Intron				
128258	G	Т	Intron				
130303	C	Α	Intron				
130617	č	A	Intron				
130910	_	Ť	Intron				
131727	C	Ť	Intron				
132895	Ž		Intron				
T35023	G	A					
133506	G	Ą	Intron				
135473	G	A	Intron				
136201	Α	A G C	Intron				
137080	Α	C	Intron				
138022	T	C	Intron				
138543	Α	Ť	Intron				
138681	C	TGA	Intron				
	_	, =	· · · · · · · · · · · · · · · · · · ·				

Context:

DNA Position

352





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[A,G]

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 [G,A]
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[T,C]

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[A,G]

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 [G,A]
- 21243 TAAATTAATCAGGGGTCACTAATCTTTGGATAATCACTCTATTGAGCTGGAACTATCCTT
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 [T,G]

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[C,T]

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[-,T]

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[T,C]

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[A,G]

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[T.C]

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[C_T]

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 [C,T]
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 [T,C]
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[T,G]





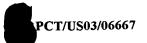
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[C,T]

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[G,A]

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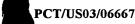
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	56/65
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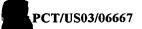
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[A.-]

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[T,A]



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[G,T]

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[C,T]

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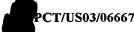
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[A,G]

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[C,T]

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[A,G]

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[G,A]

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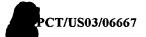
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[C,A]

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[G,A]

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138681





SEQUENCE LISTING

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WO 03/076644





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3120

3180

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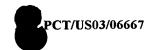
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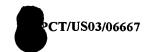
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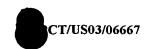
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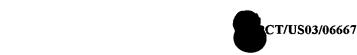


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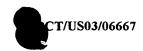
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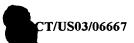


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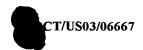
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## <213> Homo Sapien

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Phe Gly Cys Arg Arg Thr Ala Val Leu Gly Ala Ala Val Gly Phe Val Gly Leu Met Ser Ser Ser Phe Val Ser Ser Ile Glu Pro Leu Tyr Phe Thr Tyr Gly Val Val Phe Ala Cys Gln Gly Cys Ser Phe Ala Tyr Gln Pro Ser Leu Val Ile Leu Gly His Tyr Phe Lys Lys Arg Leu Gly Leu Val Asn Gly Ile Val Thr Ala Gly Ser Ser Val Phe Thr Ile Leu Leu Pro Leu Leu Arg Val Leu Ile Asp Ser Val Gly Leu Phe Tyr Thr Leu Arg Val Leu Cys Gly Cys Ser Phe Ala Tyr Gln Pro Ser Leu Val Ile Leu Gly His Tyr Phe Lys Lys Arg Leu Gly Leu Val Asn Gly Ile Val Thr Ala Gly Ser Ser Val Phe Thr Ile Leu Leu Pro Leu Leu Leu Leu Val Gly Leu Tyr Thr Leu Arg Leu Cys Ser Gly Cys Ser Phe Ala Tyr Gln Pro Ser Leu Val Ile Leu Gly His Tyr Phe Lys Lys Arg Leu Gly Leu Val Asn Gly Ile Val Thr Ala Gly Ser Ser Val Phe Thr Ile Leu Leu Pro Leu Leu Gly Asn Leu Thr Ser Thr Val Gly Leu Cys Tyr Thr Leu Arg Ile Leu Cys Gln Ile Phe Met Phe Val Leu Phe Leu Ala Gly Phe Thr Tyr Arg Pro Leu Ala Thr Ser Thr Lys Asp Lys Glu Ser Gly Gly Ser Gly Ser Ser Leu Phe Ser Arg Lys Lys Phe Ser Pro Pro Lys Lys Ile Phe Asn Phe Ala Ile Phe Lys Val Thr Ala Tyr Ala Val Trp Ala Val Ile Phe Met Phe Val Leu Phe Leu Ala Gly Phe Thr Tyr Arg Pro Leu Ser Lys Lys Glu Ser Ser Ser Phe Ser Arg Lys Ser Pro Pro Lys Lys Ile Phe Asn Phe Ala Phe Lys Thr Ala Tyr Ala Val Trp Ala Ser Ile Phe Met Phe Val Leu Phe Leu Ala Gly Phe Thr Tyr Arg Pro Leu Val Pro Ser Ser Lys Glu Lys Glu Ser Glu Asp Ser Arg Ser Ser Phe Phe Ser Arg Arg Lys Leu Ser Pro Pro Lys Lys Ile Phe Asn Phe Ala Leu Phe Lys Glu Thr Ala Tyr Ala Val Trp Ala Ala Gln Gly Ile Pro Leu Ala Leu Phe Gly Tyr Phe Val Pro Tyr Val His Leu Met Lys His Val Asn Glu Arg Phe Gln Asp Glu Lys Asn Lys Glu Val Val Leu Met Cys Ile Gly Val Thr Ser Gly Val Gly Arg Leu Leu Phe Gly Arg Ile Ala Asp Tyr Val Pro Gly Val Lys Lys Gly Ile Pro Leu Ala Leu Phe Gly Tyr Phe Val Pro Tyr Val His Leu Met His Val Glu Arg Phe Asp Asn Lys Glu Val Met Cys Ile Gly Val Thr Ser Gly





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945					950					955					960.
Lys	Ser	Gly	Ile	Pro	Leu	Ala	Leu	Phe	Gly	Tyr	Phe	Val	Pro	Tyr	Val.
•		_		965					970					975	
His	Leu	Met	Asn	His	Val	Lys	Glu	Arq	Phe	Lys	Asp	Val	Asn	Asn	Lys
			980					985			-		990		
Glu.	17a l	T.011		Met	Cva	Tle	Glv		Thr	Ser	Glv	Val		Arg	Len
GIU	Vai	995	F 11C	1100	Cys	110	1000		*****		01,	1005	_	9	LCu
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Leu		_	arg	TTE	Ата			Leu	Pro	GIY			гÀв	Gln	vaı
	1010					1015		_	_	_	1020		_		
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	2		1060	_	•		_	1065					1070		
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FIIC	GIU	1075		GLY	AIG	UIII	1080		DCI	0111	•	1085		01	
				Dh -	T1-	<b>a</b> 1			<b>W</b>	Mot	T10			Crea	Co
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_	<b>~</b>	1155			<b>~</b> 3	<b>-</b>	1160		<b>~</b> 1	<b>~</b>	D)			<b>T</b> 1 -	M-4
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1185 Ala Pro Ala Cys Leu 1265 Leu	Ile Pro Phe Phe 1250 Leu Leu Ile	Gly Tyr 1235 Ile Gly Asp Gly Ser	Phe Ala 1220 Leu Pro Phe Lys Gly 1300 Ala	Leu 1205 Gly Ala Trp Met Leu 1285 Ala	Leu  Gly  Ile  Ser  1270 Gly  Val	Gly Leu Val His 1255 Ile Ser Leu	Phe Arg Pro 1240 Ser Pro Tyr Cys Leu	Met 1225 Pro Lys Met Asp Ile 1305 Leu	Ser 121( Lys Leu Lys Thr Ala 129( Pro	1195 Ile Leu Ile Gln Val 1275 Phe Trp	Gly Gly Arg 1260 Gly Tyr	Met Ser Gly 1245 Ala Pro Leu His Ser	Thr Tyr 1230 Ala Ile Pro Ala Ser 1310 Ile	Val 1215 Asp Val Gly Ala Gly 1295 Lys	1200 Gly Val Leu Phe Gly 1280 Pro
1185 Ala Pro Ala Cys Leu 1265 Leu Pro Gln	Ile Pro Phe Phe 1250 Leu Leu Ile Arg	Gly Ile Tyr 1235 Ile Gly Asp Gly Ser 1315	Phe Ala 1220 Leu Pro Phe Lys Gly 1300 Ala	Leu 1205 Gly Ala Trp Met Leu 1285 Ala	Leu  Gly  Ile  Ser  1270  Gly  Val	Gly Leu Val His 1255 Ile Ser Leu Phe	Phe Arg Pro 1240 Ser Pro Tyr Cys Leu 1320	Met 1225 Pro Lys Met Asp 11e 1305 Leu	Ser 1210 Lys Leu Lys Thr Ala 1290 Pro	1195 Ile Leu Ile Gln Val 1275 Phe Trp Phe	Fro Gly Gly Arg 1260 Gly Tyr Ile	Met Ser Gly 1245 Ala Pro Leu His Ser 1325	Thr Tyr 1230 Ala Ile Pro Ala Ser 1310 Ile	Val 1215 Asp Val Gly Ala Gly 1295 Lys	1200 Gly Val Leu Phe Gly 1280 Pro Lys
1185 Ala Pro Ala Cys Leu 1265 Leu Pro Gln	Ile Pro Phe Phe 1250 Leu Leu Ile Arg	Gly Ile Tyr 1235 Ile Gly Asp Gly Ser 1315 Gly	Phe Ala 1220 Leu Pro Phe Lys Gly 1300 Ala	Leu 1205 Gly Ala Trp Met Leu 1285 Ala	Leu  Gly  Ile  Ser  1270  Gly  Val	Gly Leu Val His 1255 Ile Ser Leu Phe Ala	Phe Arg Pro 1240 Ser Pro Tyr Cys Leu 1320 Gly	Met 1225 Pro Lys Met Asp 11e 1305 Leu	Ser 1210 Lys Leu Lys Thr Ala 1290 Pro	1195 Ile Leu Ile Gln Val 1275 Phe Trp Phe	Fro Gly Gly Arg 1260 Gly Tyr Ile Met	Met Ser Gly 1245 Ala Pro Leu His Ser 1325 Lys	Thr Tyr 1230 Ala Ile Pro Ala Ser 1310 Ile	Val 1215 Asp Val Gly Ala Gly 1295 Lys	1200 Gly Val Leu Phe Gly 1280 Pro Lys
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1185 Ala Pro Ala Cys Leu 1265 Leu Pro Gln Thr	Phe Phe 1250 Leu Ile Arg Val 1330 Asp	Gly Ile Tyr 1235 Ile Gly Asp Gly Ser 1315 Gly Leu	Phe Ala 1220 Leu Pro Phe Lys Gly 1300 Ala Pro Ala	Leu 1205 Gly Ala Trp Met Leu 1285 Ala Ile Pro	Leu Leu Gly Ile Ser 1270 Gly Val Gly Val	Gly Leu Val His 1255 Ile Ser Leu Phe Ala 1335 Leu	Phe Arg Pro 1240 Ser Pro Tyr Cys Leu 1320 Gly Ala	Met 1225 Pro Lys Met Asp 11e 1305 Leu Leu Gly	Ser 1210 Lys Leu Lys Thr Ala 1290 Pro Gly Leu	1195 Ile Leu Ile Gln Val 1275 Phe Trp Phe His	Gly Gly Arg 1260 Gly Tyr Ile Met Asp 1340 Pro	Met Ser Gly 1245 Ala Pro Leu His Ser 1325 Lys Phe	Thr Tyr 1230 Ala Ile Pro Ala Ser 1310 Ile Leu Ile	Val 1215 Asp Val Gly Ala Gly 1295 Lys Pro Gly	1200 Gly Val Leu Phe Gly 1280 Pro Lys Met Ser Gly 1360
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1185 Ala Pro Ala Cys Leu 1265 Leu Pro Gln Thr Tyr 1345 Ala	Phe Phe 1250 Leu Leu Ile Arg Val 1330 Asp Val	Gly Tyr 1235 Ile Gly Asp Gly Ser 1315 Gly Leu Leu	Phe Ala 1220 Leu Pro Phe Lys Gly 1300 Ala Pro Ala Cys	Leu 1205 Gly Ala Trp Met Leu 1285 Ala Ile Pro Phe Leu 1365	Leu Leu Gly Ile Ser 1270 Gly Val Gly Val Tyr 1350 Ile	Gly Leu Val His 1255 Ile Ser Leu Phe Ala 1335 Leu Pro	Phe Arg Pro 1240 Ser Pro Tyr Cys Leu 1320 Gly Ala	Met Asp 1225 Pro Lys Met Asp 11e 1305 Leu Cly Ile	Ser 1210 Lys Leu Lys Thr Ala 1290 Pro Gly Leu Ile	Ile Ile Leu Ile Gln Val 1275 Phe Trp Phe His Pro 1355 Ser	Gly Gly Arg 1260 Gly Tyr Ile Met Asp 1340 Pro Lys	Met Ser Gly 1245 Ala Pro Leu His Ser 1325 Lys Phe	Thr Tyr 1230 Ala Ile Pro Ala Ser 1310 Ile Leu Ile Gln	Val 1215 Asp Val Gly Ala Gly 1295 Lys Pro Gly Gly	1200 Gly Val Leu Phe Gly 1280 Pro Lys Met Ser Gly 1360 Gln
1185 Ala Pro Ala Cys Leu 1265 Leu Pro Gln Thr Tyr 1345 Ala	Phe Phe 1250 Leu Leu Ile Arg Val 1330 Asp Val	Gly Tyr 1235 Ile Gly Asp Gly Ser 1315 Gly Leu Leu	Phe Ala 1220 Leu Pro Phe Lys Gly 1300 Ala Pro Ala Cys	Leu 1205 Gly Ala Trp Met Leu 1285 Ala Ile Pro Phe Leu 1365 Thr	Leu Leu Gly Ile Ser 1270 Gly Val Gly Val Tyr 1350 Ile	Gly Leu Val His 1255 Ile Ser Leu Phe Ala 1335 Leu Pro	Phe Arg Pro 1240 Ser Pro Tyr Cys Leu 1320 Gly Ala	Met Asp 1225 Pro Lys Met Asp 11e 1305 Leu Cly Ile	Ser 1210 Lys Leu Lys Thr Ala 1290 Pro Gly Leu Ile His 1370 Lys	Ile Ile Leu Ile Gln Val 1275 Phe Trp Phe His Pro 1355 Ser	Gly Gly Arg 1260 Gly Tyr Ile Met Asp 1340 Pro Lys	Met Ser Gly 1245 Ala Pro Leu His Ser 1325 Lys Phe	Thr Tyr 1230 Ala Ile Pro Ala Ser 1310 Ile Leu Ile Gln	Val 1215 Asp Val Gly Ala Gly 1295 Lys Pro Gly Gly Arg 1375 Leu	1200 Gly Val Leu Phe Gly 1280 Pro Lys Met Ser Gly 1360 Gln
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1185 Ala Pro Ala Cys Leu 1265 Leu Pro Gln Thr Tyr 1345 Ala Glu Asn	Phe Phe 1250 Leu Leu Ile Arg Val 1330 Asp Val Ile Gln	Gly Ile Tyr 1235 Ile Gly Asp Gly Ser 1315 Gly Leu Leu Ser Asn 1395	Phe Ala 1220 Leu Pro Phe Lys Gly 1300 Ala Pro Ala Cys Lys 1380 Ser	Leu 1205 Gly Ala Trp Met Leu 1285 Ala Ile Pro Phe Leu 1365 Thr	Leu Leu Gly Ile Ser 1270 Gly Val Gly Val Tyr 1350 Ile Thr Leu	Gly Leu Val His 1255 Ile Ser Leu Phe Ala 1335 Leu Pro Gly Ser	Phe Arg Pro 1240 Ser Pro Tyr Cys Leu 1320 Gly Ala Trp Lys Ser 1400	Met Asp 1225 Pro Lys Met Asp 11e 1305 Leu Gly Ile Glu 1385 Ser	Ser 1210 Lys Leu Lys Thr Ala 1290 Pro Gly Leu Ile His 1370 Lys Ser	Ile Ile Leu Ile Gln Val 1275 Phe Trp Phe His Pro 1355 Ser Met Gly	Fro Gly Gly 1260 Gly Tyr Ile Met Asp 1340 Pro Lys Glu Met	Met Ser Gly 1245 Ala Pro Leu His Ser 1325 Lys Phe Lys Phe 1405	Thr Tyr 1230 Ala Ile Pro Ala Ser 1310 Leu Ile Gln Met 1390 Lys	Val 1215 Asp Val Gly Ala Gly 1295 Lys Pro Gly Gly Arg 1375 Leu	1200 Gly Val Leu Phe Gly 1280 Pro Lys Met Ser Gly 1360 Gln Glu Glu



